MAY 6 1947

Vol. 105
No. 2731

Pages 457-482

May 2, 1947

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Science

THE SCIENTISTS NEWSWEEKLY

Enrico Fermi and Sir Robert Robinson, recipients of the 1947 Franklin Medals, awarded at Medal Day ceremonies of The Franklin Institute, Philadelphia, on April 16. Drs. Fermi and Robinson are shown with Henry B. Allen, executive vice-president and secretary of the Institute (left) and Richard T. Nalle, president of the Institute (right).

Published by the
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Shortage of Scientific and Technical Personnel

Kenneth A. Meade

FOR RAPID, ACCURATE ELECTROLYTIC DEPOSITIONS

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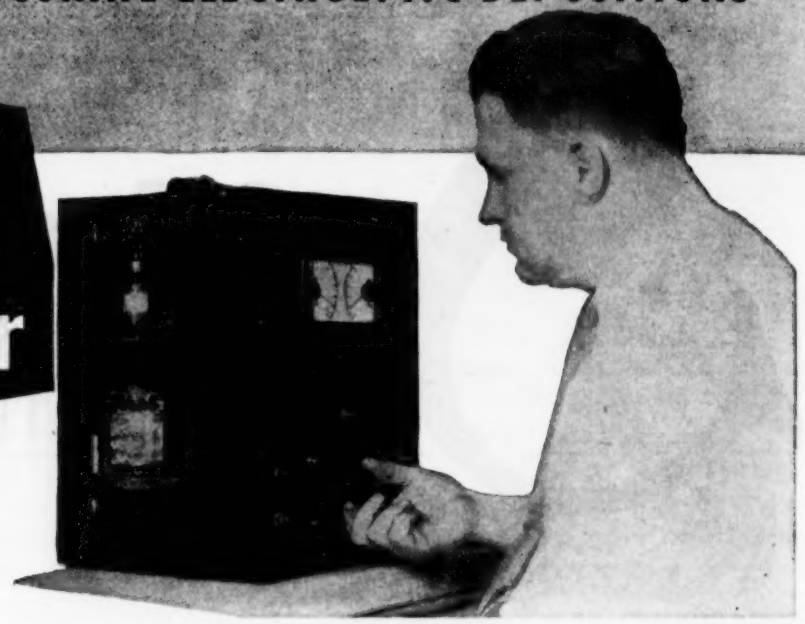

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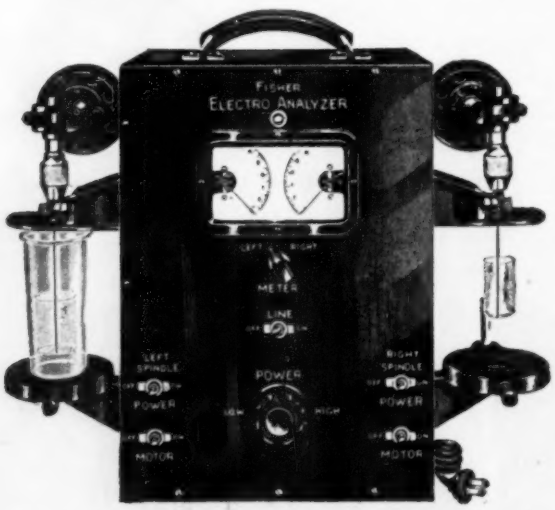

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Science

Vol. 105 No. 2731 Friday, May 2, 1947

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(*Cover photo by Gladys Muller, Philadelphia.*)

Science a weekly journal, is published each Friday by the American Association for the Advancement of Science at Mt. Royal & Guilford Avenues, Baltimore 2, Maryland. Founded in 1880, it has been since 1900 the official publication of the AAAS. Editorial, Advertising, and Circulation Offices, 1515 Massachusetts Avenue, N.W., Washington 5, D. C. Telephone, EXecutive 6060 or 6061. Cable address SCIMAG, Washington, D. C.

Articles offered for publication should be sent to the Editor, 1515 Massachusetts Avenue, N.W., Washington 5, D. C.

Membership correspondence for the AAAS should be sent to the Administrative Secretary, 1515 Massachusetts Avenue, N.W., Washington 5, D. C.

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Entered as second-class matter January 17, 1947, at the postoffice at Baltimore, Maryland, under the act of March 3, 1879.

The Shortage of Scientific and Technical Personnel:

What Industry Is Doing About It

Kenneth A. Meade, *Director of Technical Employment, General Motors Corporation, Detroit, Michigan*

IN PRESENTING THE VIEWPOINT OF INdustry with respect to the shortage of scientific and technical personnel I would first like to raise three questions: Is the shortage of such personnel, from a long-range standpoint, as acute as we have been led to believe? Is not the real shortage one of suitability of such personnel for technical employment rather than one of numbers available for employment? Finally, should not our attack on the problem be aimed at development of scientific and technical personnel who are well qualified to succeed in the field rather than at turning out a greater number of such people, many of whom will not remain long in technical work?

Today our economy is so integrated that anything which affects one element in turn affects most of the other phases. Our economy has become increasingly technical. National defense, public utilities, agriculture, and industry have become more and more dependent on scientists and engineers for their survival and their growth to meet the increased demands put on them.

I believe that the situation in the automotive industry, with which I am most familiar, is quite typical of that found in industry as a whole. In the early days of the industry the average plant was small. New products and improvements in products already in production were largely the result of work done by inventors. These men did not necessarily follow any organized program in producing new developments, but, as they tried new ideas and found that they worked, they put them into production. Sometimes the ideas were good, and the product sold, but, if the idea was poor, the product was apt to be a failure. As evidence, think back to names of some of the automobiles built in the first decade of this century which are only memories today. As a rule, however, these earlier products were rather primitive according to our present standards. The improvements and advancements that could be made were fundamental and obvious. Thus, inventors working without any particular plan could show progress.

At that time each unit of product was manufactured and produced on an individual basis. The parts were made by craftsmen using the standard tools of the machine shop and employing the skills of the toolmaker and machinist. These parts were fitted and assembled by skilled mechanics working on a complete unit until it was finished. Little thought was given to manufacturing processes and better production methods as we know them today. Consequently, the cost of these early automobiles was high, and the demand for them was small.

But, as automobiles became more popular and the demand increased, manufacturers had to find surer ways of improving the product and cheaper methods of producing it. Better-organized product development, mass-production methods, and the assembly line came into being. The individual parts were made as nearly alike as possible so that they could be used interchangeably in assembling the product and to facilitate its repair in service.

This fundamental shift in the way the business was carried on required changes in method and changes in the kind of personnel needed. The scientist and the engineer replaced the inventor; trained and experienced designers were needed; and toolmakers, diemakers, and other skilled craftsmen made the tools to build the product instead of the parts of the product itself. These parts could now be made by men with less skill, each trained to run a specialized machine designed to do a particular job. The finished parts were assembled into units and these units into the final product on assembly lines by men also trained to do their particular jobs. The industry became more specialized, plants grew larger, and those with responsibility for developing the product, planning the manufacturing methods, and managing the business were required to have more technical knowledge and ability.

So, today, in modern industry an increased number of men with scientific and technical backgrounds, obtained through either formal education or experience, is essential to its functioning. Refinements and advances that can be made in the product and processes are smaller and more difficult to attain than in the first years of the industry. As a result, scientists and engineers now have to plan more carefully and use the techniques of the laboratory to carry on organized programs of research and development on materials, manufacturing methods, and processes in order that the product of the future will be better and can be built at a lower cost. Sometimes these research programs result in complete new industries that further

An address delivered before the Symposium on the Shortage of Scientific Personnel, AAAS Boston Meeting, December 28, 1946.

increase the demand for scientific and technical personnel. New models of the product are designed, developed, and completely tested before they are put into production. Many of the men who supervise the building of the product have to have technical knowledge and skills to solve the day-to-day technical problems of production. In addition, the men who lay out the plants and plan the best routing of material and parts, as well as those who service the products in the field, need some technical training to do their jobs effectively.

There is an additional factor that, from our standpoint, contributes a great deal to the shortage of scientific and technical personnel. This is the problem raised by a sizable number of men who are trained in college for scientific and technical work and who, after a brief period of employment in the field, leave it to enter some totally unrelated type of occupation. These moves are usually made by individuals who believe they will find greater immediate returns for themselves in relation to happiness in the work, pay, or opportunities for advancement in the new activity. However, our experience has indicated that the reason may be a more fundamental one. Many of the men who make these changes are not fitted physically, mentally, or temperamentally for scientific or technical employment or, perhaps we should say, are better fitted in these respects for some other field of endeavor, and so they tend to gravitate away from technical work in their search for satisfactory employment. Whatever the reason, this group is to be found in every graduating class in every engineering college or technical school and reduces the number of men who are potential for the scientific and technical responsibilities in our future economy.

There are some contributions that industry can make in arriving at a solution to this problem of a shortage of scientific and technical personnel. However, a satisfactory and complete solution can be best obtained through the joint efforts of the educational institutions and employers of scientific and technical personnel toward achieving a better mutual understanding of the responsibilities involved.

In the first place, industry can do very little to increase the number of technical people immediately available for employment. This is largely the responsibility of the colleges and universities, and, since it takes considerable time to give science and engineering students their basic educational backgrounds, not much can be done to hasten the process. The immediate shortage is due to the fact that during the war years not as many young men were given an opportunity to prepare for scientific and technical work as in the years prior to the war.

However, while this immediate shortage in numbers of technical men available for employment exists, industry is doing certain things which help to relieve its effect. Veterans who went into military service immediately following the completion of a college or university course in science and engineering are being employed in positions for which we ordinarily recruit new graduates. Included in this group are many who were trained in military service educational courses, such as the Navy V-12 program. Men with scientific and technical backgrounds who were employed during the war years in temporary war jobs are being employed wherever possible. Maximum recognition is being given to the professional training of the experienced scientists and engineers already in our organizations in relation to their job assignments, in order that they may use their "know-how" most effectively. Quasi-technical employees, such as draftsmen, laboratory assistants, and experimental project mechanics, are found among veterans who obtained some specialized training in these fields while in the service as well as those who wish to go into industrial "on-the-job" training programs in these areas. All of these steps are aimed at the placement of technical and scientific employees in industrial positions where they can make their greatest individual contributions in relation to their particular backgrounds of education and experience. These efforts will help to spread the available supply of technical talent where it is most needed in industry until the present shortage is relieved in a few years by the graduation of larger classes now starting their science and engineering courses in our colleges and universities.

But from a long-range standpoint the problem is deeper than that of a shortage in the number of people educated for employment in these areas. There is also the problem of lack of ability to handle an industrial technical assignment among individuals who have passed the educational course requirements for this kind of employment but who do not possess the other qualifications needed. As I see it, the solution of this problem involves two things: better selection of those to be educated for industrial employment, and development of an attitude in the graduate that will help him to find his place in the industrial scheme more quickly.

Every field of work has rather definite requirements of knowledge and skills as well as of mental and physical abilities; every job requires some capacity to handle human relations problems; and every job requires specific interests on the part of the one who does it and should satisfy certain desires and ambitions on his part. Since the professional technical and scientific employees of industry are a part of management, their jobs have the added requirement that, to qualify to fill them, an individual must have the background on which to develop a management viewpoint and method of attack on problems.

So, to find the right person for a job we must find the applicant who has all the attributes required by that job. Some may argue that anyone can do any job to which he puts his mind, and this may be true in the exceptional case. However, most of us are better qualified for one particular field of work than for some other, and it is in

this field that we as individuals can make our greatest contributions to our employers, society, and ourselves.

A college degree in engineering, physics, or chemistry or good grades in specific courses are not enough unless the individual possesses the other abilities—the mental discipline, the capacity for dealing with people, and the interests the job requires. Only when we place on a job the individual who has all the attributes required in that job will we have an employee who is happily placed, will do his most effective work, and hence make the greatest contribution to the organization employing him. By making that contribution he will benefit himself. Therefore, the student who is interested in science or engineering should be assisted in analyzing himself and the fields of work for which he wishes to qualify. By the time he is graduated he should know what he has in the way of abilities, human relations attributes, interests, and desires that have been developed so far and will thus be in a better position to determine in what field he should seek employment—teaching, research, production, technical sales, etc.

What is the responsibility of our educational institutions in this connection? I believe that most of us will agree that for the majority of industrial jobs in the technical field an employee needs a good educational grounding in fundamentals rather than a highly specialized background. There are, of course, the exceptions of some highly specialized research and design jobs. He needs a good working knowledge of the physical sciences, mathematics, design, the laws of economics, and the psychology of human relations. He must be able to express himself clearly and forcefully either orally or in writing. An individual in whom the college or university has instilled this fundamental background should not be limited in his outlook or in the type of industrial job in which he can successfully develop.

But these are only his tools. He must learn how to use these tools. He must learn how to think clearly. Any curriculum in science or engineering should so prepare the graduate that he can apply the same scientific method of analysis to the solution of such problems as those of production, industrial relations, and business economics as he does when working a problem of research, design, or development. Industry is sometimes criticized by educators for not recognizing the professional status of all the graduate engineers in its employ because some of these are found several years after graduation in technicians' jobs that could just as well be handled by people with less training. The graduate engineer or scientist who, after he gains experience and knowledge, does not have the ability to solve major problems in the industrial field is no more a professional man than the doctor who graduates in medicine but cannot pass the state medical board examinations to practice.

Technical colleges and universities have the added responsibility of using the techniques developed by the psychologist and others who have specialized in the study of the behavior of people for better selection of those students who have the greatest aptitude for success in the fields of science and engineering. They have the responsibility of counseling their students and assisting them in analyzing themselves in preparation for their selection of the field of employment in which they have the best chance for success.

Each industry has the responsibility of furnishing the technical schools with pertinent information in regard to its policies, management philosophy, products, geographical scope, financial standing, and the educational backgrounds and attitudes expected in the graduates it employs. Industry is responsible for carefully analyzing its technical and scientific jobs in regard to the abilities, skills, human relations attributes, and interests required in each one and in regard to the personal desires each one will satisfy and for furnishing this information to the schools for student guidance purposes. Industry can inform the technical graduate about its training programs, benefit plans, and the opportunities it offers to a man with a technical background.

Industry also has the responsibility of training those graduates it employs and assisting them in bridging the gap between supervised development in the college classroom and self-development on an industrial job. Some such training must be furnished, since the colleges and universities cannot be expected to train individuals for specific industries. Industry, therefore, is responsible for furnishing the new employee with information on the products, processes, operating principles, and procedures of its organization. Through conferences with members of management he should have an opportunity to learn their methods of operation, philosophy, and point of view in preparation for the responsibilities that may lie ahead. In addition, during this preparatory period of employment he should be given working experience in the various phases of work related to the job and department for which he has been employed. Such a program, whether formal or informal, gives the employer a better opportunity to observe the performance of the individual in order to assist him in finding the specific field of work for which he is best qualified to make the greatest contribution in the years to come. While emphasis is put on intensive training during the first few years of employment and whenever the employee is transferred or promoted to a new job or another unit of the organization, it does not stop there. It takes a long time to learn the art of management, so his training, no matter how informal, will continue as long as he stays with the organization and grows in ability to assume greater responsibility. For this training to be effective, the graduate cannot start with an antimanagement point of view for, if he does, he sabotages the organization from inside.

General Motors feels that proper training of all employees is a very necessary part of its personnel program.

Each division has set up training programs to fit its individual needs. The importance of training is indicated by the fact that a central training agency—General Motors Institute—has been in operation at Flint, Michigan, for more than 25 years. The staff of the Institute assists the divisions and operating units in analyzing their training needs and in the design, development, and administration of programs to meet those needs. Management training for shop foremen and other first-line supervisors has been given considerable emphasis and has proved invaluable in developing an efficient organization. The Institute also operates a cooperative college course in Industrial and Mechanical Engineering which each year furnishes our various plants with more than 150 graduates, each trained for specific responsibilities in the technical and manufacturing phases of the business.

Training helps the employee to orient himself to the organization and to learn to apply whatever fundamental educational background he has to the job at hand and to the ones that lie ahead. It is one of the best ways of assisting the employee in getting the most out of his job.

With the cooperation of industry the colleges and universities should be able to do a better job of student selection and counseling, so that those who are graduated and enter the technical and scientific fields will have a better chance of success and will be more apt to make a career of these fields.

In addition, there is the problem of developing in the technical or scientific student an attitude needed for industrial employment. After all, he is not recruited as a factory laborer or into a routine job in which he will spend the rest of his life. He is employed because management believes he has possibilities for development into a management position himself. A willingness to work on any phase of the job to be done, a willingness to accept criticism and suggestion, a willingness to become a part of management and to accept the responsibilities of management are all a part of this attitude.

In order to give a better idea of what we mean by attitude as it relates to the college graduate going into industry I would like to quote from a talk given by William E. Wickenden, president of the Case School of Applied Science, at the General Motors Institute Commencement in August 1946:

> . . . But there is another thing, which seems far more important, which you can do uniquely perhaps, and that is to make the process of education bridge over the gap between school and practice in which so many men seem to lose the momentum of intellectual mastery and professional growth. The most important thing anyone can learn in school is not some collection of items of knowledge or tricks of skill, but the art of carrying on his own education without a teacher's supervision and the conveyor belt of a curriculum and academic schedule. That art, I regret to say, we too often fail to develop or, if we do, it will too often fall a casualty in the first few months out of college. . . .

Finally, it is most important that the graduate have a firm belief and complete confidence in the policies and management methods used in the organization he joins and that he be motivated not only by what he hopes to gain personally from the company but also by a desire to make a contribution to it. It is fundamental that, if any student leaves college with the opinion that the present system of industrial management is subject to serious question, he will have great difficulty in fitting into and becoming an effective part of the management group. If this is not his objective, he should not look to industry for his opportunities.

Unfortunately, not all members of college or university faculties have had an opportunity to gain industrial experience and, as a consequence, not all of them are prepared to give their students a very realistic picture of what to expect when they take industrial jobs. Many men in technical or management positions in industry have not had an opportunity to obtain a firsthand knowledge of the problems of the engineering school. Too often their opinions of educational courses or of a particular educational institution are based on hearsay or an unfortunate experience with a few poorly prepared college graduates. Some of them feel that students are often taught courses dealing with the way the instructor or textbook writer would like to have industry do a job rather than courses explaining how it is actually done. We cannot expect members of the college faculties to give their students anything of management's viewpoints unless they have been given an opportunity themselves to study at firsthand and appraise these viewpoints as they are applied in different companies. I believe that conferences between educators and men in industry who employ technical graduates, where information is exchanged and where college courses and industrial training programs are constructively criticized, will do a great deal toward the solution of these problems. Faculty members would then be better equipped to develop in their students a broader and more realistic viewpoint and prepare them to make the shift from college into the industrial field more readily. Industrial management will be better informed as to the backgrounds of education and attitudes of the graduates they employ and more sympathetic toward their problems of orientation to industry.

During the last two years we have held short summer conferences of our management with educators in the fields of industrial relations and personnel. The purpose of these is to give a group of college and university men who are teaching courses in labor relations and related subjects an opportunity to observe at firsthand our methods of handling problems in these areas. At each conference the educators first met with members of our personnel staff. Next each educator was sent to one of the company's plants and given an opportunity to observe for several days any phases of the personnel program and to discuss his observations with members of plant man-

agement. Finally, the group returned to Detroit and, after spending a day exchanging ideas obtained from their plant visits, presented their comments and suggestions to interested members of our Corporation management, the personnel staff, and personnel representatives from our divisions and plants.

In order to give a greater number of educators an opportunity to gain this kind of experience so that they will be in a better position to present their students with a more realistic picture of what they can expect when they accept industrial employment, this experiment should not be confined to one company or one field of education. We should consider its application or the application of other methods to the fields of science, engineering, finance, and distribution, among others.

I firmly believe that by pooling the experience and "know-how" of employers with that of faculty members and administration of our colleges and universities we will find better ways of producing technical and scientific graduates who are better qualified to do their jobs and more interested in making these fields a career wherever they choose to accept employment. This cooperative attack from a long-range point of view will, it seems to me, help to insure more effective use of technical and scientific graduates in industry. This may be more important than producing a larger number of graduates, many of whom leave this field of work after they are trained for it. Let us put greater emphasis on producing quality rather than on just increasing the number of graduates in the technical and scientific fields.

The Scope of Science

Robert M. Yerkes

Yale University, New Haven, Connecticut

WHEN, SOME MONTHS AGO, I FIRST read the paragraphs in British publications which provide the text and motivation for this article, I was so amazed and dismayed by what seem to me partially erroneous and wholly misleading statements that I felt impelled to make immediate reply. But on further reflection, being of a noncontroversial disposition and much averse to giving my time to expression of disagreement, I inhibited the impulse. Recently there have been developments which brought the matter to my mind again, and this time with such sense of duty and opportunity that I am now offering critical rejoinder and alternative view. Unwillingly I write in the first person, since I may not assume that the British writers speak for their scientific colleagues or the British people, and since I have no mandate to represent my scientific colleagues and my fellow citizens of the United States of America.

The first half of my text appears in the following paragraph from an editorial entitled "The method and scope of science," published in "a quarterly review designed to record the progress of the sciences in the service of mankind," which is "made and printed in Great Britain." The journal is called *Endeavour*.

> It is, however, in the realm of qualities not susceptible of measurement of any kind that the scientific method—as far as it has yet developed—ought frankly to be recognized as *inapplicable*. An obvious example can be taken from the field of art. The scientific method can give a great deal of information on the chemical nature of pigments, on the wavelength of the light they reflect, and on similar factors, but *it is wholly unable to predict* whether a picture will have an aesthetic appeal to those who see it. *Nor can the scientific method be of help* in those problems rse lating to drama, literature, and the like, which involve *qualitie that cannot be measured* and knowledge which is not communicable. In the wide field of human affairs *the scientific method cannot be applied*, even in the form of statistical analysis, to problems in which events are influenced by the philosophical values of goodness, truth, and beauty, and emotions such as patriotism, fear, or political conviction (*Endeavour*, 1946, **5**, 126). [Italics by R. M. Y.]

In this emphatic statement of opinion I should wish, on the basis of my knowledge of fact, to convert all the negatives—the impossibles and improbables—into positives. Thus "inapplicable" becomes "applicable"; "it is wholly unable to predict" becomes "it is partially able to predict"; "nor can the scientific method be of help" becomes "the scientific method can be of help"; "qualities that cannot be measured" becomes "there are no qualities of natural phenomena which cannot be measured, although at present there are many which are not being measured or are measured very crudely and inaccurately"; and "the scientific method cannot be applied" becomes simply "the scientific method can be applied to all natural phenomena."

Actually, what the writer of the editorial deems impossible I have observed being done in what chances to be my country, culture, and sphere of creative scholarship, on all sides and increasingly throughout my life. For nearly 50 years most of my time and intellectual resources have been devoted to efforts, sometimes recognized as successful, to do just what is termed impossible

or improbable. Under the circumstances, it would require much more than an exhibit of authoritarian belief or emphatic assertion of individual opinion to convince me—and I am sure that in this I may speak for hundreds of my scientific colleagues and associates—that what I have observed by way of research endeavor and progress is illusory, and that we who are working as biologists and social scientists are not achieving dependable and serviceable results in our varied studies of behavior, experience, social relations, and institutions. If the natural phenomena designated by such terms are not amenable to systematic study by procedures which are in principle the same as those employed in the physical sciences, hosts of us who now are classified as scientists actually are self-deceived workers who, unlike our physical science colleagues, are denied access to the truth concerning the natural phenomena which particularly interest us.

My proof? As exhibit in support of the positive statements which I have made, I offer simply the literature of technical report and general discussion classified under functional biology, psychology and psychobiology, anthropology, sociology, and other so-called social science categories. I have in mind, as especially pertinent, the literature of the 20th Century. It seems idle to cite titles from our numerous journals, monograph series, and books. With regret I admit that I am a bit suspicious that the negatives of the editorial, and the writer's obvious lack of faith in the applicability of scientific procedures to psychological and social phenomena, indicate ignorance of this vast array of recent discovery and of technical applications in various branches of human engineering. Perhaps there is also a tendency to look backward in the history of science instead of examining current activities and, with that as vantage ground, trying to look forward optimistically and prophetically. Assuredly, history, and especially the history of science and of man, is invaluable for our guidance, but its making is far more exciting and fate determining than is mere recording or subsequent rewriting. One dislikes to admit that he appears to be living in another world of fact and striving than that of his opponent, and I earnestly hope that the writer of this editorial and I shortly may discover that we both are scientists in spirit and achievement and may come to agree that assertion or prediction of the impossible is an unprofitable exercise in our callings which not infrequently makes one appear foolish to one's successors. I cannot even be so charitable as to wish that I may come to accept the point of view or faith of this writer, for I am reasonably sure that he is mistaken, and I hope to convince him, and all who sympathize with him, of that fact!

As to the second half of my text, less words of comment are required since it is a specific exhibit which might have been used in *Endeavour* in support of the general negations. I borrow it from an important report of effort to further human welfare by application of dependable knowledge. *The Peckham experiment*, by Innes H. Pearse and Lucy H. Crocker, physician and social worker, respectively, commands my admiration and, apart from such exceptional disagreement as I herein note, my enthusiastic approval. It deserves to be widely read, and it should become influential. My interest in the book led me months ago to urge that it be made available in an American edition. Perhaps if I knew the authors as well as I now know their experimental outlook and services, I should not have the heart to criticize them! The paragraph to which I wish to take exception is entitled "The Place of Psychology in the Peckham Experiment." It reads thus:

> One last word. The Centre has often been accused of neglecting Psychology. In our opinion, however, there is as yet no psychology; only a knowledge of psycho-*pathology*. Indeed, how can there be a scientific study of psychology until an experimental field for the *study of the healthy* has been established? At present, knowledge of the physiology of the psychological mechanism lags far behind its pathology which fills libraries, for all knowledge so far available on this subject is derived from the disordered, and its theories and technique are devoted to remedy. Remedy is important for the sick, but the sick are not the primary concern of the Centre. Once however a medium is found in which we can watch the action-pattern of function in the family unit, we are presented with an experimental field in which we can begin to look for a psychology based upon health rather than pathology (*The Peckham experiment: a study of the living structure of society*. New Haven: Yale Univ. Press, 1945. Pp. 272–273).

The assurance and finality of statement in this case are devastating. As a psychobiologist whose affiliations and services for a half-century have been primarily medical, and as one who recognizes the existence and value of psychology as extension of physiology to include the whole of human behavior and experience, I am deeply sympathetic because of the disadvantages under which the authors of this report labored. By their own statement, it is in a land and culture in which, apart from psychopathology, there is no science of psychology. But in this matter, what of the world situation? And what, I apprehensively ask myself, will the thousands of American psychologists, my colleagues and co-workers, think and say when they read: "In our opinion, however, there is as yet no psychology." Will they respect the efforts of our British co-workers for human welfare, or will they instead say that such ignorance, narrowness of view, and provincialism are inexcusable? Science generally is considered international, and it certainly should be reasonably independent of local advantages and disadvantages.

In this case also I offer as eloquent exhibit to disprove the authors' negatives the world's literature of psychological science and especially that of America during the current century. Reports of research progress are to be found in a score of technical journals and other serials. Our handbooks, manuals, encyclopedias of psychological fact, method, and generalization are many. In America psychopathology is recognized as special development

from, and an important part of, the science of normal behavior-experience. If the various divisions of biology, functional and structural, are entitled to acceptance as natural sciences of measurement and prediction, then, from the facts provided by these exhibits, we must grant that psychology actually exists as science. Moreover, whether or not we chance to be medically trained or interested especially in psychopathology, we psychologists and psychobiologists are working in the spirit, with the objectives, and, in principle, with the methodologies of the other physical and biological natural sciences.

Obviously, my disagreement with the authors of *The Peckham experiment* is absolute. Nevertheless, as scientists we all are committed to strive for progress, and most of us recognize that what today appears impossible may be achieved tomorrow. I should like to suggest, if it be not presumptuous, that either the Crown or the Prime Minister of Great Britain appoint a commission of experts to visit the United States of America expressly to inquire into the existence and status of the "impossible" sciences of human behavior-experience, social organization, and institutions, and to report authoritatively and informatively to the people of Great Britain. Belief and action should not depend upon the assertions of the editors of *Endeavour*, of the authors of *The Peckham experiment*, or of an American scientist who refuses to admit that it is impossible for any one person to be physicist, biologist, sociologist, all in one, and to seek always to advance knowledge and human welfare as *scientist*, sometimes as *specialist*.

On the Multiple Factor Theory of Respiratory Control as Outlined by Gray

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A RECENT ARTICLE ON A MULTIPLE factor theory of control of respiratory ventilation (*4*) carries certain wide implications for which the author did not present the necessary substantiating data. Furthermore, many of the statements seem highly questionable, if not erroneous; e.g. a categorical statement that all preceding theories of control have "consistently met with failure" is presented without evidence.

Gray states that Gesell's theory "avoided the objections to the arterial H-ion theory" and that "the improvement, however, is more apparent than real, for the H-ion concentration of the cells of the respiratory center is still beyond measurement." If this statement means that Gesell's theory is difficult to handle quantitatively, we must agree. Otherwise, the meaning is not clear.

There is a considerable body of evidence that respiratory center acidity and chemoceptor acidity run parallel to respiratory minute volume. Cerebrospinal fluid acidity (*2*) offers a first approximation of central nervous system acidity. These approximations have been abundantly supported by observations on venous blood acidity. Present information on central nervous system chemistry and metabolism permits related deductions concerning the acidity of the center (*7*). Whatever method is employed to appraise intracellular acidity of the respiratory center and chemoceptors, the premise that intracellular acidity plays an important role in the control of respiratory ventilation is supported (*2*).

Gray seems to have accepted the views of Gesell on this major issue of intracellular acidity, for he writes as follows:

> The second step in the application of the multiple factor principle is to decide at what point the concentrations of the three chemical agents are to be measured. Although ideally their concentrations should be measured in the respiratory center and the peripheral chemoreceptors where they exert their effects, this is not feasible.

This is a point which cannot be passed over lightly, for if one fact is established with reasonable certainty, it is the lack of correspondence between the concentration of H-ions and of CO_2 in the arterial blood and the volume of respiratory ventilation. Of all the points of concentration, arterial blood is the least informative. Yet Gray states that "the most feasible approach is to correlate respiratory ventilation with the arterial concentration of the three chemical agents, bearing in mind the possibility that difficulties may arise in transitory unsteady states and in conditions of seriously altered blood flow."

It is a well-known fact that venous blood is usually more acid than arterial blood and that the increase in

H-ion concentration occurring as it passes through the tissue is due to the addition of acid metabolites to the blood by the tissues. Gesell and his co-workers have clearly shown that hemorrhage increases the difference in H-ion concentration of venous and arterial blood. Despite a decrease of H-ion concentration of arterial blood of pH 0.1 or more, due to augmented ventilation of the blood in the lungs, both the venous blood and the cerebrospinal fluid turn more acid than normal as a result of hemorrhage (*6*). Such exaggeration of differences in H-ion concentration of arterial and venous blood is not so transitory as Gray seems to imply and throws considerable light on the mechanisms of respiratory control. Yet Gray is of the opinion that "venous blood levels are unsuitable because of the extreme variability in the composition of venous blood. Neither mixed venous blood nor blood from any accessible vein reliably reflects conditions both within the respiratory center and in outlying chemoreceptors. The only remaining possibility is arterial blood." It is one matter to use the H-ion concentration of the arterial blood to meet the convenience of the investigator. It is another matter, as Gray himself has pointed out, to select the site of concentration which throws most light on the mechanisms involved in the control of respiratory ventilation. If one uses the H-ion concentration of the arterial blood because it reflects the acidity of the respiratory center, as Gray in one place implies, it is somewhat illogical at another place in the line of reasoning to consider the H-ion concentrations of the arterial blood as the stimulating agent. Gray's dilemma increases on realization that the volume of pulmonary ventilation varies inversely as the H-ion concentration of the arterial blood in a number of important types of hyperpnea, and in some of these the carbon-dioxide pressure is low and the oxygen pressure high.

Gray's Chemical Ventilation Equation

The chemical ventilation equation as given by Gray (*4*) is:

$$VR = 0.22H + 0.263pCO_2 - 18.0 + \frac{105}{10^{0.038pO_2}}.$$

Such an equation is a device to predict the magnitude of the ventilation when H, pCO_2, and pO_2 are known. But we doubt very much, unless independent substantiating evidence is presented, that the equation can be used to establish causal relationships or provide information on the mechanisms by which H, pCO_2, and pO_2 are related. While the algebraic device is simple to handle from the standpoint of the mechanical manipulations of the data, it is not necessarily better than other devices, and other devices should be avoided only after proof is presented that they are less reliable than the algebraic device. A rigid mathematical analysis will also give a product which can be used to predict respiratory volume. The problem is which prediction will give the smallest relative or absolute error. The equation to be favored is the one giving the most accurate prediction. Among the equations deserving investigation are (1) and (2), formulated by Krueger.

$$(1) \qquad y = ax^by^cz^d \text{ or } \text{Log } y = \text{Log } a + b \text{ Log } x + c \text{ Log } y + d \text{ Log } z$$

$$(2) \qquad y = ab^xc^yd^z \text{ or } \text{Log } y = \text{Log } a + x \text{ Log } b + y \text{ Log } c + z \text{ Log } d$$

$$\text{or Log } y = A + Bx + Cy + Dz.$$

None of the equations, including Gray's, has any value unless the probable or standard error of the prediction is also known. One can predict the magnitude of ventilation even without knowing what is meant by volume of respiration; but here the probable error of the guess is exceedingly great. A prediction is valueless unless one can associate with it a standard error and thus provide some concept of the validity of the prediction. Gray has neglected to include the standard error with his equation. Further, Gray's equation would be of value only where it can validly be used. Gray defines the realm of validity as any condition where H, pCO_2, and pO_2 of the arterial blood, operating normally, are controlling respiration. But what are the criteria that only these three factors and not others, such as muscle and other reflexes, pain, body temperature, or metabolism, are influencing respiration? When do these factors operate *normally*? The validity of a predicting equation also depends upon the source and quantity of data from which it is derived, and Gray has not published this information.

As a reason for avoiding a product of H, pCO_2, and pO_2 for the prediction of the magnitude of ventilation, Gray has said that taking the product of partial effects implies synergistic action, and that such a procedure should be avoided until actual evidence of synergism is encountered. If this were true, his own equation should also be avoided, because that equation implies synergism. Synergism usually is defined as a working in the same direction. In his equation the H, pCO_2, and pO_2 components are always positive and hence always *arithmetically* as well as *algebraically additive*. Since the three components always act in the same direction, they are, by definition, synergistic. If one is to consider Gray's equation as a functional mathematical equation rather than a prediction equation, one wonders how the constant -18.0 is to be interpreted. The constant can be separated into three components, each to be associated with the H, CO_2, or O_2 component, and thus provide the possibility

for negative partial effects related to the H, CO_2, and O_2 components. Yet one must keep in mind that (1) the arterial hydrogen ions and carbon dioxide are presumed to stimulate in proportion to their concentrations; (2) the oxygen always gives a positive component which is less, the higher the oxygen concentration; and (3) the effects of the H, pCO_2, and pO_2 components are always positive, no matter what negative constant is associated with them. This difficulty could be eliminated by establishing arbitrary zero lines for H, CO_2, and pO_2 and using a more complex function of these components; but Gray has neglected to do this. Hence, if one accepts his formula as a functional mathematical equation, one must conclude that the effects of H, O_2, and CO_2 are arithmetically additive (always positive) and hence synergistic, that these factors operate on a center whose nonstimulated condition represents a value of -18.0, and that the sum of the O_2, CO_2, and H components must reach 18.0 before ventilation occurs. A more logical attitude is to treat Gray's equation as a pure prediction equation. If we know something of the H-ion concentration, the arterial O_2, and the arterial CO_2, we can make a prediction regarding the magnitude of the ventilation.

Beyond presenting his prediction equation, Gray's only suggestion, offered without proof, is that certain factors may act independently. Gray holds that "if it were true that only one of the two agents [CO_2 or H-ion concentration] is the true stimulus, the procedure used to establish the equation [4] would have betrayed the fact by emerging with a coefficient of zero for the inactive agent." In order to reduce this argument to an absurdity, an equation will now be derived from Gray's equation where the coefficient of CO_2 is zero; then, if we were willing to follow the logic of Gray, we could conclude that it was not the CO_2 and H-ions of the arterial blood, but rather the bicarbonate ions and the H-ions which were the true respiratory stimuli. From the law of chemical equilibrium,

$$(3)\quad [H^+] \times [HCO_3^-] = K_1 \times [H_2CO_3] = K_2 \times pCO_2 \quad (5).$$

Hence,

$$(4)\quad pCO_2 = [H^+] \times [HCO_3^-]\, K_3,$$

and substitution in Gray's equation yields Equation 5.

$$(5)\qquad VR = 0.22H + 0.263 \times K_3 \times [H^+] \times [HCO_3^-] - 18.0 + \frac{105}{10^{0.038pO_2}}.$$

In Equation 5 the coefficient of CO_2 is zero. Because we do not attach any functional significance to either Gray's equation or Equation 5, we continue to believe that the blood carbon dioxide *influences* respiration.

Gray uses his equation to predict the relationships in passive muscular exercise. He assumes that the passive nature of the exercise prevents any change in metabolic rate. The metabolism during passive exercise is readily amenable to evaluation and should be evaluated experimentally before assuming that metabolism will not be changed. Since the experiments of Cohnheim on *Sipunculus* and of Cohnheim and Von Uexküll on the leech showed that the energy consumption is greater in these animals when loaded than when unloaded (*1*, p. 538), it is possible that the changes in tension and length may produce an increase in metabolism during passive exercise. Hence, one cannot as yet take at face value the calculation which associates no change in metabolism with a decrease from 40 to 29 mm. Hg in the blood carbon-dioxide pressure, a change in pH from 7.41 to 7.52, and an increase of 40 per cent in ventilation during passive exercise.

Comments on Nielsen's Theory

Nielsen (*9*) views CO_2 as the unique stimulus for respiration and assumes that the irritability of the respiratory center to this stimulus is variable. CO_2 produces a greater increase in respiration per unit change in the pH of the arterial blood than is produced by other acids. Gray categorically claims that a unique potency of CO_2 is denied by the fact that both acid and CO_2 increase respiration. He seems to overlook the fact that injection of acid causes an increase in CO_2 and that CO_2 could be the effective factor in producing an increase in respiration. We would like to comment further that there is some similarity between Nielsen's theory, invoking the unique stimulus of CO_2 acting upon a center whose irritability varies, and that of Gesell, which relates the changes in respiration to tissue acidity and to the acetylcholine concentration at certain key points. If the irritability in Nielsen's theory were defined in terms of bicarbonate and acetylcholine content, the two theories would be very closely related. In that acetylcholine and acidity are more clearly defined entities than irritability, it is easier to think in terms of Gesell's theory than of Nielsen's. The latter theory is a reflection of early similar statements by Loewi (*8*) and others.

Classification of Theories of Respiratory Control

Careful over-all consideration of the adjustment of breathing leads to the inescapable realization that a very large number of factors—many more than are usually considered—must participate in the control of respiratory ventilation. Gesell (*2*) and Gesell and Hansen (*3*) have emphasized this point in their papers. If it is true, as these authors have suggested, that the electrogenic properties of acetylcholine may provide the activating forces of the respiratory center, the heterogeneous factors contributing to the control of breathing become

resolvable into a final common factor, namely, concentration of free acetylcholine in the respiratory center. Synaptic bombardment of the respiratory center by impulses originating in chemoceptor endings, in pain endings, in proprioceptive endings of the lungs, of respiratory muscles and locomotor muscles, and impulses originating in the higher centers should lead to liberation of acetylcholine in the center. Increased acidity of the center resulting from any of many possible causes should, by its anticholinesterase activity, potentiate the effects of prevailing bombardment of the center. Theoretically, an increase of H-ion concentration and of CO_2 concentration and a decrease of O_2 concentration of the arterial blood should increase the acidity of the tissue. Thus, these three factors, which Gray has emphasized, are theoretically resolvable into the single factor, tissue cH. The view that both increased bombardment of the center and increased intracellular cH lead to increased concentration of acetylcholine offers an extremely simple theory for explaining respiratory ventilation. Because a host of heterogeneous factors must be theoretically resolvable into a final common factor such as neurocellular electrotonic currents, however, is no reason for identifying Gesell's theory as a single factor theory. If there be need of classifying theories of respiratory control into single and multiple factor theories, Gesell's theory should be included with the latter. A quantitative elaboration of all the factors to which Gesell has called attention is a more difficult problem. Although much quantitative data concerning the regulation of respiration are available, any inclusive formulation which would account for the many factors and their interactions becomes extremely cumbersome. On the other hand, necessary simplification renders any such formulation hypothetical.

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Reply to Krueger's Criticism of the Multiple Factor Theory

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A THUMBNAIL SKETCH OF RESPIRATORY theories will be of assistance to the reader whose only recent information on the subject consists of Krueger's article. Early theories which postulated a *single arterial stimulus* for respiration have long been realized to be incompatible with experimental observation. Later theories, which have added a second postulate, that a number of factors influence the *sensitivity* of the respiratory center to the unique arterial stimulus, are also at variance with experimental observation. A third type of theory, such as Gesell's *original* theory, which postulated that ventilation is controlled by a single *immeasurable* stimulus, namely, the intracellular pH of the respiratory center, is impossible to quantitate. In order to avoid these difficulties, the multiple factor theory postulates that a *number of stimuli* exert individual effects on ventilation; that the levels or concentrations of these stimuli are frequently influenced by one another; and that, as a result, the actual ventilation represents the algebraic sum of the partial effects of the separate stimuli. The logical implications of these postulates have been worked out in detail and given quantitative mathematical expression; they have been applied to very extensive and well-known experimental data and found to give excellent agreement and to provide a greatly enhanced understanding of the control of respiration. All these details have been presented in a series of seven wartime reports (*1–5*), totaling some 220 pages, released from the AAF School of Aviation Medicine. The *Science* article (*6*) which Krueger criticizes constituted a brief summary of the principles and general nature of the theory.

The multiple factor theory, like any other theory in science, can be legitimately criticized on the grounds that it fails to correspond to experimental observation, or that it is logically inconsistent with itself, or that it is not verifiable. Few of Krueger's criticisms fall into any of these categories, as may be seen from the following criticisms and answers:

(1) Krueger's opening sentence claims that necessary substantiating data were not presented. This accusation is made a number of times. The facts are that extensive substantiating data were presented in the wartime reports (*1–3*) (available on request) given as references in the *Science* article, but which Krueger has ignored. More

detailed evidence of the failure of preceding theories is also included in these reports.

(2) In his second paragraph Krueger states that the only interpretation he can make of my criticism of Gesell's (original) theory is that it is difficult to handle quantitatively. This interpretation is correct. Is it an error to consider unsuccessful a theory which is not amenable to quantitative expression, but which, nevertheless, treats of quantitative events? Krueger implies that my criticism of Gesell's *original* theory was leveled at Gesell's *modern* theory. In fact, the main theme of Krueger's paper is the defense of Gesell's modern views against my supposed attack. This defensive effort would have been more appropriate had there been any actual attack. I can do no better than quote my original words (*6*):

> This modified theory [Gesell's] is no longer primarily a theory of the over-all regulation of respiration [in contrast to the multiple factor theory]; rather, it is primarily a theory concerning the intracellular mechanisms by means of which certain agents, involved in the control of respiration, bring about stimulation or activation of receptor and effector cells. The two types of theory, however, are neither mutually exclusive nor competitive, but complementary.... It is important to distinguish clearly between the over-all regulation of respiration for homeostatic purposes and the intimate cellular mechanisms involved.... Like thermodynamics, it [the multiple factor theory] is concerned with the beginnings and ends of processes and not with intervening steps, however important the latter may be from other standpoints.

(3) Krueger registers numerous objections to the use of arterial blood levels of the chemical stimuli.

(a) One objection is based on the claim that arterial levels are least informative because it has been established that they do not correlate with ventilation. What had already been established was that no *single* arterial agent correlates with ventilation; what I have established on the basis of experimental data is that *multiple correlation* between ventilation and the *several* arterial agents is quite good.

(b) Another objection is based on the allegation that arterial levels were chosen "to meet the convenience of the investigator" instead of to "throw more light on the mechanisms involved in the control of respiration." Arterial levels were admittedly selected because they are more feasible to measure; my preference for accomplishing the feasible rather than speculating on the infeasible seems not to be shared by Krueger. Having selected a feasible procedure, it thereby became possible to discover that it threw more light on the control of respiration. The justification for this selection consists of the fact that it led to the discovery of a multiple correlation between arterial levels and ventilation.

(c) Krueger accuses me of inconsistency in considering the arterial H-ion to *reflect* the acidity in the respiratory center in one place and in another to *be* the respiratory stimulus itself. The fact is that I did and do consider the arterial pH in many important conditions to be a measurable index of the effective pH, whatever the value of the latter may be and regardless of its site of action.

(d) Krueger implies that I have not considered situations in which arterial and cellular pH's may be dissociated. The truth is that I have considered some of these conditions in considerable detail (*2, 4*).

(4) Krueger also devotes a number of pages to criticism of the chemical ventilation equation.

(a) Doubts are expressed that it "can be used to establish causal relationships." The fact is that no equation ever established causal relationships, and this one was not intended to do so. If one must think in anthropomorphic terms, it might be pointed out that the chemical ventilation equation describes the "causal" effect of arterial pCO_2 on ventilation, and the formal ventilation equation describes the "causal" effect of ventilation on the arterial pCO_2, thus for the first time explicitly clarifying certain confusing "causal" relationships in respiration.

(b) Doubts are also expressed that the equation can "provide information on the mechanisms by which H, pCO_2, and pO_2 are related." These doubts are well founded; the equation does not and was not intended to do this. A group of three other equations were provided for this purpose.

(c) Krueger objects to the chemical ventilation equation because other "equations deserving investigation" were not explored. As a matter of fact, the chemical ventilation equation represents the only one among a number explored which was found to describe the experimental data. It must be confessed, however, that no attempts were made to fit exponential or logarithmic equations to linear data!

(d) Krueger also objects to the algebraic summation device on the grounds that simple arithmetic summation is all that is required. The thread of the argument at this point becomes incoherent. He says that the equation "provides the possibility for negative partial effects" and, further on, that from the equation "one must conclude that the effects of H, O_2, and CO_2 are arithmetically additive (always positive)." The first of these contradictory statements is the correct one. The confusion finally culminates in Krueger's explicitly redefining "synergistic" as synonymous with "additive," thereby enabling the conclusion to be drawn that my expressed preference for additive effects (my definition) is really a preference for synergistic effects (his definition) when I profess to shun synergistic effects (my definition).

(e) Krueger undertakes to demonstrate the "absurdity" of my statement, viz., that the procedure used to establish the chemical ventilation equation would have yielded a zero coefficient if either H-ions or pCO_2 *alone*

were influencing ventilation. It is pertinent to remark that the procedure employed was not described in the *Science* report which Krueger read. His "demonstration" consists of replacing $BHCO_3$ for pCO_2 in the equation, leaving *two* essential variables still present, and thus confirming my statement that one variable alone does not account for the experimental data.

(5) Krueger takes exception to my analysis of the respiratory response to exercise because I assumed that metabolism is not increased by passive exercise. This analysis was adequately labeled as incomplete and preliminary; the tentative nature of the *quantitative* values was indicated. The *qualitative* validity of the conclusions requires only that passive exercise produce less increase in metabolism than in ventilation in comparison with active exercise.

(6) It is claimed that in referring to Nielsen's theory I state "categorically" that a unique potency of CO_2 is denied by the fact that Nielsen obtained a response to both acid and CO_2. My statement was that the occurrence of responses to both agents denied the conclusion Nielsen drew from them, namely, that only *one* was a potent stimulus. Krueger further states that I "overlooked" the fact that the injection of acid causes hypercapnia, which could be responsible for the respiratory response to the acid. The truth is that I have analyzed the acute responses to injected acid in detail (*4*). Unfortunately, Krueger seems to have "overlooked" the fact that Nielsen did *not* inject acid, but fed NH_4Cl and that he observed *acapnia* (as have all others) and not hypercapnia.

The title I selected for my theory has turned out to be an unfortunate one, in that it does not adequately distinguish it from other theories. The consequences have been that the theory is superficially judged to be no different from others, since its title can be appropriately applied to others. Many theories have included multiple *factors* presumed to operate by controlling the concentration of a unique stimulus or by controlling the sensitivity of the respiratory center to a unique stimulus. The multiple factor theory differs from these in that it postulates multiple *stimuli* exerting individual or partial effects. Gesell's and Nielsen's theories, therefore, are appropriately classified as multiple factor theories, and mine might better have been called the multiple stimulus theory.

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Chemical Research Conferences, AAAS, 1947:

Colby Junior College, New London, New Hampshire, June 16–August 22

W. George Parks, *Director,*
Rhode Island State College, Kingston

INFORMATION ON THE CHEMICAL RESEARCH Conferences for 1947 with respect to location, purpose, and registration was published in the preliminary announcement in *Science* (March 14, 1947).

Requests for attendance at the Conferences or for any additional information should be addressed to W. George Parks, Department of Chemistry, Rhode Island State College, Kingston, Rhode Island. From June 15 to August 20, 1947, mail should be addressed to Colby Junior College, New London, New Hampshire.

The final program follows:

Organic High Polymers

C. C. Price, Chairman; W. O. Baker, Vice-Chairman

June 16 C. S. Marvel, "New Monomers for Synthetic Rubber"; R. L. Frank and Norman Rabjohn, "Structure of Synthetic Rubbers."

June 17 G. S. Whitby, "Proliferous Polymerization of Butadienes"; John Rehner, Jr., "The Polyisobutylene Reaction."

June 18 A. J. Warner, "New Polymers"; H. Mark, "Cyclo-octotetraene."

June 19 A. V. Tobolsky, "Aging and Degradation of Polymers"; E. H. Farmer, "Thermally-promoted Olefinic Reactivity and Polymerization."

June 20 M. G. Evans, The University, Leeds (tentative).

Catalysis

Walter G. Frankenburg, Chairman; H. S. Taylor, Vice-Chairman

June 23 Aristid V. Grosse, "Concept of Catalytic Chemistry"; H. S. Taylor, "New Data on the Heterogeneity of Catalytic Surfaces."

June 24 James B. Sumner, "Chemical Nature of Biocatalysts; Problems Concerned With the Isolation of Enzymes"; Paul H. Emmett, "Adsorption of Carbon Monoxide and Hydrogen on Carbided Iron Catalysts."

June 25 Otto Beeck, "Thermodynamic and Mechanical Statistical Aspects of Catalysis"; Thomas W. DeWitt, "Mechanism Studies with C^{14} on Iron Fischer-Tropsch Catalysts"; P. W. Selwood, "Magnetochemistry and the Structure of Catalytically Active Solids."

June 26 Marion Armbruster, "Sorption of Gases on a Plane Surface of Stainless Iron-Chromium-Nickel Alloys at 20°, −78°, and −185°C."; M. Jellinek, I. Frankuchen, R. Ward, and M. Erchak, "X-Ray Diffraction in the Study of Catalysts."

June 27 Herman E. Ries, Jr., "Adsorption Studies of Some Supported Catalysts and Their Supports."

Petroleum

W. G. Lovell, Chairman; O. Beeck, Vice-Chairman

June 30 F. D. Rossini, "Hydrocarbons in Petroleum"; S. S. Kurtz, "Analysis of Petroleum Products for Hydrocarbon Types."

July 1 H. M. Smith, "Survey of Composition of American Petroleums"; A. C. Fieldner, "Synthetic Fuels and Shale Oil."

July 2 Clark Goodman, "Physical and Chemical Changes Produced by Nuclear Radiations"; A. M. Rothrock, "Power Production From Petroleum."

July 3 J. R. Bowman, "Theory of Distillation and Related Separation Processes"; Manson Benedict, "Diffusion Separation Processes."

July 4 O. Redlich, "Azeotropic and Extractive Separations."

Textiles

W. A. Sisson, Chairman; Ross C. Whitman, Vice-Chairman

July 7 Eugene Pacsu, "Molecular Structure of Cellulose and Its Relationship to Chemical Degradation"; Clifford B. Purves, "Some Aspects of the Chemical Reactivity of Cellulose."

July 8 John A. Howsmon, "Fine Structure, Moisture Regain, and Physical Properties of Rayon"; R. F. Nickerson, "Reaction of Cellulose With Formaldehyde Compounds and Its Effect on Fiber Properties."

July 9 Alfred E. Brown and Milton Harris, "Natural Protein Fibers"; Harold P. Lundgren, "Synthetic Protein Fibers."

July 10 Charles F. Goldthwait, "Swelling of Cotton and Its Utilization in Water-resistant Fabrics"; J. H. Dillon, "Harold DeWitt Smith Memorial Program"; A. K. Schneider, "Sorption of Acid Dyes by Nylon."

July 11 Earl K. Fischer and Charles H. Lindsley, "Rheological Properties of Compositions Used in the Textile Industry."

Corrosion

K. G. Compton, Chairman; I. A. Denison, Vice-Chairman

July 14 H. H. Uhlig, "Electrochemical Theory of Corrosion"; R. B. Mears, "Factors Affecting the Rate of Atmospheric Corrosion."

July 15 W. S. Loose, "Atmospheric Corrosion of Light Metals"; R. H. Brown, "Atmospheric Corrosion of Light Metals"; A. W. Tracy, "Atmospheric Corrosion of Nonferrous Metals"; W. E. Campbell, "Indoor Atmospheric Corrosion of Nonferrous Metals."

July 16 Harry R. Copson and W. O. Binder, "Atmospheric Corrosion of Iron and Ferrous Alloys"; C. H. Sample, "Atmospheric Corrosion of Metallic Protective Coatings."

July 17 I. A. Denison, "Underground Corrosion"; R. B. Hoxeng, "Cathodic Protection of Underground Structures by Means of Light Metals."

July 18 R. L. Starkey, "Bacteria and Underground Corrosion"; Paul Weir, "Water Supply Corrosion Tests; A Ten-Year Progress Report."

Medicinal Chemistry

E. H. Northey, Chairman; J. M. Sprague, Vice-Chairman

July 21 Enzyme Chemistry: Carl Vestling, "General Survey"; Sherman Dickman, "Fatty Acid Oxidation"; I. C. Gunsalus, "Transformations of Amino Acids"; M. E. Krahl, "Enzymes for Carbohydrate Utilization in Animal Tissue."

July 22 Antibiotics: Karl Folkers, "Chemistry of Streptomycin"; C. J. Cavallito, "Antibiotics From Plants"; O. Wintersteiner, "Some Aspects of Penicillin Chemistry."

July 23 (*a*) Curare and Curare-like Drugs, (*b*) Folic Acid: J. D. Dutcher, "Chemistry of Curare Alkaloids"; A. R. McIntyre, "Theories of Curarization"; James M. Smith, Jr., "Chemistry of Folic Acid and Related Substances."

July 24 Veterinary Medicine: W. A. Hagan, "Problems for Chemotherapeutic Research in Veterinary Medicine"; A. O. Foster, "Incidence and Treatment of Parasitic Diseases"; Emanuel Waletzky, "Chemotherapy of Coccidiosis."

July 25 Tuberculosis: Guy P. Youmans, "Testing of Tuberculostatic Agents *in Vitro* and in the Mouse"; W. H. Feldman, "The *in Vivo* Evaluation of Substances Effective Against the Tubercle Bacillus."

Vitamins

D. W. Woolley, Chairman; Floyd S. Daft, Vice-Chairman

July 28 P. L. Harris and E. L. Hove, "Treatment of Experimentally Induced Stomach Ulcers With Tocopherol"; N. B. Guerrant, "Recent Developments in Vitamin A Standardization and Assay"; W. Trager, "A Fat-soluble Substance With Biotin Activity and Its Relation to the Course of Avian Malaria."

July 29 H. R. Bird, "Studies on an Unknown Growth Factor in Cow Manure"; C. A. Cary and A. M. Hartman, "I. Evidence of the Existence of a Still Unidentified Growth Factor in the Nutrition of the Rat. II. Relation Chemically and Nutritionally to Protein, and Occurrence in Variously Prepared Caseins and Other Sources of Protein"; D. W. Woolley, "Strepogenin."

July 30 W. E. Knox, "Identification of New Metabolites of Nicotinic Acid"; D. M. Bonner, "Precursors in the Biosynthesis of Nicotinic Acid"; G. Goldsmith and H. P. Sarett, "Interrelationship of Tryptophane and Nicotinic Acid Metabolism in Man."

July 31 J. Schultz and G. T. Rudkin, "Requirements for Growth of *Drosophila* on the Chemically Defined Medium"; G. Fraenkel, "Nutritional Requirements of Insects"; C. N. H. Long, "Relation of Ascorbic Acid to Adrenal Cortical Function."

August 1 W. D. Salmon, D. H. Copeland, and R. W. Engel, "Production of Neoplasms as a Result of Prolonged Choline Deficiency"; T. Gillman, "Pathological Reactions Encountered in the Livers of Malnourished South African Negroes, With Some Observations on the Response of the Hepatic Lesions to Therapy as Revealed by Serial Aspiration Biopsies."

Food and Nutrition

Lawrence Atkin, Chairman; P. L. Harris, Vice-Chairman

August 4 Gerald J. Cox, "Caries and Nutrition in Human Subjects"; James H. Shaw, "Diet and Experimental Caries"; Discussion leader, Philip Jay. Curt P. Richter, "Self-Selection of Diets"; Heinrich Waelsch, "Nutrition and Brain Function"; Discussion leader, Edward M. Scott.

August 5 H. N. Brocklesby and C. E. Lane, "Some Aspects of the Physiology of Vitamin A"; Discussion leader, H. Sobotka. Walter O. Lundberg, "Food Antioxidants—Fat Soluble"; Roy W. Riemenschneider, "Water-soluble Antioxidants"; Discussion leader, Philip L. Harris.

August 6 Abraham White, "Nutrition and Endocrine Function"; Paul György, "Diet, Liver and Sex Hormones"; Discussion leader, to be announced. Lemuel D. Wright, "Intestinal Microorganisms and Animal Nutrition"; Milicent L. Hathaway, "Intestinal Synthesis of Food Factors Essential for Human Nutrition"; Discussion leader, to be announced.

August 7 M. L. Anson, "Sugar-Protein Reaction, Significance and Methodology"; Earl R. Stadtman, "Chemistry of the Sugar-Protein Reaction"; Discussion leader, J. P. Kass. Donald K. Tressler, "Enzymes in the Food Industry"; Z. I. Kertesz, "Pectins and Pectic Enzymes"; Discussion leader, Carl R. Fellers.

August 8 H. H. Mitchell, "Evaluation of Proteins and Hydrolysates *in Vivo*"; R. J. Block, "Evaluation of Proteins and Hydrolysates *in Vitro*"; Discussion leader, D. Melnick.

Cancer

A. M. Brues, Chairman; Paul S. Henshaw, Vice-Chairman

August 11 Chairman, A. M. Brues. W. H. Summerson, H. Gilder, and J. M. Lee, "Metabolic and Enzymatic Characteristics of Lymphosarcoma"; Symposium on Nucleic Acid Metabolism, Samuel Graff and Hardin B. Jones.

August 12 Chairman, Paul C. Aebersold. Symposium on Radioactive Isotopes in Therapy of Malignant Disease. Paul F. Hahn and C. W. Sheppard, "Radioactive Colloidal Sols"; Rulon W. Rawson, "Radioactive Iodine"; Byron E. Hall, "Radioactive Phosphorus"; Anna Goldfeder, "Radiation Effects on Normal and Malignant Tissues."

August 13 Chairman, Chester Stock. Round Table Discussions on Methods and Results in Chemotherapy of Malignant Disease, Joseph Burchenal, B. E. Hall, D. A. Karnofsky, Robert Mellors, Richard Ormsbee, F. S. Philips, E. B. Schoenbach, C. L. Spurr, K. Sugiura.

August 14 Chairman, Gray H. Twombly. Symposium on Carcinogenic Action of Acetylaminofluorene, K. E. Paschkis and A. Cantarow; H. P. Morris, C. S. Dubnik, T. B. Dunn, J. W. Thompson and B. B. Westfall, V. Suntzeff, "Influence of Aging on Development of Epidermal Cancer"; Roy Hertz, "Inhibition of Estrogen-induced Tissue Growth by Progesterone."

August 15 Chairman, Paul S. Henshaw. Mark W. Woods and H. G. DuBuy, "Similarity of Action of Chondriogenes and Viruses"; P. A. Gorer, "Antibody Responses in Transplanted Tumors."

Instrumentation

C. O. Fairchild, Chairman; J. C. Peters, Vice-Chairman

August 18 Robert B. Jacobs, "High-Vacuum Measurement and Control"; R. L. Garman, "Physical Properties Not Commonly Used in Indirect Measurement"; C. M. Albright, Jr., and C. H. Neilsen, "Unsolved Control Problems of the Chemical Industry."

August 19 Ralph H. Müller, "Electronics in Modern Analytical Chemistry"; Donald P. Campbell, "Practical Application of Automatic Control Theory"; Ralph E. Clarridge, "Organization and Functions of an Application Engineering Department."

August 20 Norman Wright, "Application of Infrared Measurements in Industry"; John J. Grebe, "Application of Control Principles to Human Behavior."

August 21 James J. Lingane, "Polarography"; J.C. Mouzon, "Low-Temperature Radiation Pyrometry in Industry."

August 22 W. J. Eckert, "Field of Usefulness of Various Mechanical and Electrical Calculators."

NEWS *and Notes*

The Franklin Institute celebrated its 1947 Medal Day at a presentation dinner in Franklin Hall, Philadelphia, on April 16 honoring 19 medalists. The highest award of the Institute, the Franklin Medal, was presented to Enrico Fermi, Institute for Nuclear Studies, University of Chicago, and Sir Robert Robinson, Oxford University, England. Dr. Fermi, who received the 1938 Nobel Prize in physics for his early work in production of transmutations by neutron bombardment, spoke briefly on the opportunities offered by recent developments in the field of nuclear physics to add to and integrate what is now known about the nature of forces within the atom. Sir Robert, who received the award for his contributions in the field of chemistry of natural substances, spoke on the value of concerted research as exemplified by the history of the development of penicillin.

The Ballantine Medal was awarded to George C. Southworth, Bell Telephone Laboratories, the Newcomen Medal, to Everett G. Ackart, recently of the Du Pont Company, the Clamer Medal, to Edgar H. Dix, Jr., Aluminum Company of America; the Brown Medal, to Karl P. Billner, Vacuum Concrete, Inc.; the Clark Medal, to Edward G. Boyer, Philadelphia Electric Company; the Wetherill Medal, to Kenneth S. M. Davidson, Stevens Institute of Technology; Henderson Medals, to Lars O. Grondahl, Union Switch & Signal Company, and Sedgwick N. Wight, General Railway Signal Company; Levy Medals, to Everett M. Barber and Jay B. Malin, both of the Texas Company, and Joseph J. Mikita, the Du Pont Company; Potts Medals, to Robert H. Kent, Aberdeen Proving Ground, and Vladimir K. Zworykin, Radio Corporation of America; Longstreth Medals, to Samuel Berman, Waugh Equipment Company, and Harold J. W. Fay, Submarine Signal Company; and Certificates of Merit, to Joseph Razek, Llanerch, Pennsylvania, and Peter J. Mulder, Shippensburg State Teachers College.

About People

Enrico Fermi, Nuclear Research Institute, Chicago, has been named honorary chancellor of Union University, Schenectady, New York, for 1947–48, an office conferred annually since 1878 on such outstanding leaders as Wendell Willkie, Bernard Baruch, Irving Langmuir, President Taft, Chief Justice Hughes, Elihu Root, Whitelaw Reid, and Senator Vandenburg.

George W. Carter, head of the Physics Department, Wayne University, since 1917, has been retired at his own request by the Detroit Board of Education.

R. W. Trullinger, chief of the Office of Experiment Stations, Department of Agriculture, has been appointed assistant administrator of the Agricultural Research Administration. Dr. Trullinger will continue as chief of the Office of Experiment Stations, so that the office will be brought into closer contact with the over-all planning of research in the Department.

James A. Noble, chief geologist of the Homestake Mining Corporation, has been granted a leave of absence by the Corporation in order to serve as professor of metalliferous geology at the California Institute of Technology, starting September 1, 1947. Dr. Noble succeeds H. J. Fraser, now general manager of the Falconbridge Nickel Mining Company.

Richard H. Daggy, formerly assistant professor of entomology at the University of Minnesota, has been appointed medical entomologist for the Arabian American Oil Company. Dr. Daggy's headquarters will be at Dhahran, Saudi Arabia.

B. S. Pickett, head of the Department of Horticulture and of the horticultural section of the Agricultural Experiment Station, Iowa State College, for 24 years, will retire June 30 but will continue as professor in the department. He will be succeeded by E. S. Haber, head of the vegetable crops subsection.

Clinton M. Osborn, Department of Anatomy, College of Medicine, Ohio State University, has been appointed associate professor of zoology, Syracuse University, effective September 1, 1947. Dr. Osborn was formerly associated with the Biological Laboratories of Harvard University, where he received his Ph.D. degree, and during the war was a Major in the Aviation Physiology service of the U. S. Army.

Robert A. Moore, professor of pathology at Washington University School of Medicine since 1939 and acting dean of the School for the past year, has been appointed dean. Dr. Moore is secretary of the American Board of Pathology and editor of the *Journal of Gerontology*. During the war he served as civilian resident consultant to the Army Medical Museum and to the Secretary of War on epidemic diseases.

Cornelia T. Snell, Snell Laboratories, New York City, will speak on "Synthetic Detergents" May 5 at The Pennsylvania State College in the annual Marie Curie Lecture Series sponsored by the Palladium Chapter of Iota Sigma Pi, national honor society for women in chemistry.

Harold C. Wiggers, associate professor of physiology, University of Illinois College of Medicine, has been appointed head of the Department of Physiology and Pharmacology, Albany Medical College, and will assume his duties on July 1.

P. J. Selgin, 35-year-old expert in high-frequency radiation and electronics, has been appointed to the staff of the National Bureau of Standards, where he will work on the development of electronic ordnance for the military services in the Ordnance Development Division.

Grants and Awards

Hubert Lyman Clark, associate professor emeritus of zoology at Harvard University, is the recipient of the 1946 Clarke Memorial Medal, one of Australia's leading scientific honors, awarded by the Royal Society of New South Wales. The medal is presented for distinguished work in the natural sciences performed in the Australian Commonwealth or its territories. Dr. Clark was "unanimously agreed upon because of the great interest in Australian zoological

problems, particularly in regard to the elucidation of the Echinodermata of the country."

Linus Pauling, director of the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, has been awarded the Theodore William Richards Medal of the Northeastern Section of the American Chemical Society. Dr. Pauling was especially cited for his work in quantum mechanics, valence theory, crystal structure, electron diffraction, and biochemistry. The award will be presented at a meeting of the Northeastern Section on May 8.

Barbara McClintock, Department of Genetics, Carnegie Institution, Cold Spring Harbor, New York, received the $2,500 achievement award of the American Association of University Women at the Association's convention in Dallas, Texas, April 18. Dr. McClintock received the award in recognition of her work in the field of cytogenetics.

Wolfgang Koehler, Swarthmore College, received the Howard Crosby Warren Medal and Award at a meeting of the Society of Experimental Psychologists on April 9. Dr. Koehler was cited "for his studies on figural after effects as an approach to a more general theory of perceptual processes."

Brig. Gen. George R. Callender, U. S. Army (retired), has been awarded the United States of America Typhus Commission Medal for exceptionally meritorious services in organizing, directing, and supporting investigations of the rickettsial diseases, in training personnel in organizing a laboratory for the study of these diseases, and in aiding and supporting the Commission.

Julian I. Gilliam has received the first in a series of fellowships to be awarded by the Virginia Cancer Foundation for a year of training in cancer work at Bellevue Hospital under supervision of New York University College of Medicine doctors.

The American Veterinary Medical Association has announced the renewal of the following fellowships for 1947–48: Howard W. Dunne, working at Michigan State College on swine enteritis; Dean S. Folse, working at the University of Minnesota on coccidiosis in turkeys; and Melvin J. Swenson, working at Iowa State College on nutrition and its effects on diseases of swine. The renewals, together with new fellowships for 1947–48 which will be announced upon acceptance by the winning candidates, were awarded by the Fellowships Committee of the Association's Research Council at a meeting in Chicago on April 12. All funds for this program are derived from contributions from veterinarians.

The American Philosophical Society has awarded fellowships from the Penrose Fund to the following candidates for their respective studies: Victor F. Hess, Fordham University, actual ionization produced by the gamma rays from well-analyzed types of rocks; L. Reed Brantley, Occidental College, acidic and oxidizing properties of oxygen fluoride in aqueous solution and in the gaseous state; Lewis H. Kleinholz, Reed College, endocrine and nervous factors in the regulation of hyperglycemia in crustaceans; Thos. A. Stephenson, University of Miami, general biology of animals and seaweeds between tide marks; George L. Kreezer, Institute for Advanced Study, determination of the components of biological systems on the basis of the mathematical analysis of transient response curves; Ching-tsao Wei, University of Nanking, (1) a survey of the seed-borne pathogens of soybean in North and Central China and (2) a study on the relative effectiveness of treatments with organic mercury dusts and hot water; David H. Raab, Brooklyn College, neurology of hearing and auditory learning in animals; and T. C. Schneirla, American Museum of Natural History, behavior pattern of army ants in relation to underlying ecological and physiological conditions.

Colleges and Universities

The University of Tennessee has announced the following appointments to its chemistry staff: Evan C. Noonan, Westvaco Chlorine Products, Inc., as associate professor, and George P. Mueller, Wyeth Institute of Applied Biochemistry, as assistant professor.

The University of Michigan has announced the following appointments for the academic year 1947–48: Donald D. Brand, professor of geography; George M. Sutton, half-time curator of birds in the Museum of Zoology and associate professor of zoology; and Richard K. Beardsley, instructor in anthropology. The following leaves of absence were also announced: Leslie A. White, professor of anthropology, for the first semester, to do research on the evolution of culture; Mischa Titiev, associate professor of anthropology, for the second semester, to make use of a grant from the Rackham Research Foundation for the study, in Chile, of the changing pattern of Araucanian culture; and Shirley W. Allen, professor of forestry, for the first semester, to do research in forest administration and in the general field of conservation of natural resources.

The University of Pennsylvania School of Medicine has announced that as of July 1, 1947, T. Grier Miller, Truman G. Schnabel, and Charles C. Wolferth, who now hold full professorships in clinical medicine, will become full professors in medicine. Francis C. Wood, assistant professor in medicine, will become full professor and chairman of the Department of Medicine, succeeding O. H. Perry Pepper, who has asked to be relieved of his administrative duties.

Summer Programs

The Franz Theodore Stone Laboratory, of Ohio State University, will offer 18 courses of advanced study in botany, entomology, and zoology during its summer quarter, beginning June 16. The station, operating as a regular department of the University, maintains a departmental library and a full-time staff. Living accommodations include a men's dormitory, a women's dormitory, and a residence hall for married students. Registration for the summer quarter will be held at the Laboratory on June 16, but those interested in attending are advised to submit applications as soon as possible to Dr. Thomas H. Langlois, Director, Franz Theodore Stone Laboratory, Put-in-Bay, Ohio.

The University of California Medical School, in association with University Extension, University of California, announces a course in the Application of Nuclear Physics to the Biological and Medical Sciences, to be given at the Medical Center, San Francisco, June 30–July 18. The course will consist of didactic lectures, laboratory demonstrations, and seminars for round-table

discussions and will be open to individuals in the fields of medical and biological research. Detailed information may be obtained from: Dr. Stacy R. Mettier, Head, Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22, California.

Duke University Marine Laboratory, Beaufort, North Carolina, is offering two courses for graduate students and qualified seniors this summer. Marine Zoology will be given during the first term, June 12–July 24, by C. G. Bookhout; Plant Ecology, during the second term, July 25–August 29, by H. J. Oosting. Opportunities for research in marine botany or zoology and local flora or fauna will be offered graduate students throughout the summer.

Industrial Laboratories

The General Electric Research Laboratory announces the appointment of Glenn T. Seaborg, professor of chemistry, University of California, and co-discoverer of the artificial element, plutonium, as a consultant in nucleonics.

Pyridium Corporation, Yonkers, New York, has announced the following appointments: John F. Reinhard, formerly with the Burroughs Wellcome Company, Tuckahoe, New York, as a pharmacologist; and Charles F. Duca, formerly instructor of bacteriology, College of Physicians and Surgeons, Columbia University, as a bacteriologist.

Elections

The New York State Archaeological Association, at a meeting at the Rochester Museum of Arts and Sciences on April 12, elected Carl E. Guthe director, New York State Museum, as president and Charles F. Goddard as first vice-president.

The Southern New England Chapter of the Soil Conservation Society of America, at its organizational meeting on March 8, elected the following officers: Ayers Brinser, chairman; Irene H. Stuckey, vice-chairman; Laurence T. Small, treasurer; and L. Russell Albright, secretary.

George R. Harrison, dean of the School of Science, Massachusetts Institute of Technology, has been elected chairman of the American Institute of Physics, succeeding Paul E. Klopsteg, director of research, Northwestern University Technological Institute, who has served as chairman since 1940.

Meetings

The American Society for the Study of Arteriosclerosis, now being organized, will hold its constituting meeting June 9 at the Hotel Strand, Atlantic City, New Jersey. Clinicians and experimentalists interest in a concerted investigation of all phases of the disease are invited to join and are urged to communicate as soon as possible with Dr. O. J. Pollak, Wilmington General Hospital, Chestnut and Broom Streets, Wilmington 14, Delaware.

The American Association of Physics Teachers and **The American Society for Engineering Education** will meet jointly at the University of Minnesota, Minneapolis, June 18–21. The program chairmen for the meeting, C. E. Bennett and J. W. Buchta, are planning a symposium on the teaching of physics, particularly as it relates to students in electrical engineering. Complete programs for the meeting may be obtained after May 10 from C. J. Overbeck, Secretary, American Association of Physics Teachers, Physics Department, Northwestern University, Evanston, Illinois. Members planning to attend the meeting are urged to make hotel reservations as soon as possible through the Hotel Association of Minneapolis.

The Acoustical Society of America will meet at the Pennsylvania Hotel, New York, May 8–10. This meeting, which will be concerned chiefly with the means of attaining closer correlation of the art of music and the science of acoustics, will feature the following speakers: Howard Hanson, Eastman School of Music, Rochester, New York; Harvey Fletcher, Bell Telephone Laboratories; Harold Burris-Meyer, Stevens Institute of Technology; Leopold Stokowski; Gustave Reese, American Musicological Society; and V. O. Knudsen, University of California, Los Angeles.

The Association of Geology Teachers will hold its annual meeting May 9–10 at Milwaukee-Downer College, Milwaukee, Wisconsin. In addition to presentation of papers, the program will include the presidential address of Neil A. Miner, Cornell College; a discussion on "What the Graduate School Expects of the Undergraduate," led by Arthur L. Howland, Northwestern University; the annual banquet and lecture; and either a field trip to Silurian and Devonian localities or a visit to the Milwaukee Public Museum. Those interested in attending should communicate with Miss Katherine F. Greacen, Secretary, Milwaukee-Downer College, Milwaukee 11, Wisconsin.

The Society of American Bacteriologists, meeting May 13–16 at the Bellevue Stratford Hotel in Philadelphia, will honor Ludvig Hektoen at its 1947 annual lecture. The lecture, which has been scheduled for the morning of May 14, will be delivered by William H. Taliaferro, University of Chicago, on "The Inhibition of Reproduction in Parasites by Immune Factors."

The Division of Solid State Physics of the American Physical Society, now in the process of formation, will meet in Montreal on June 21, according to an announcement by the Organizing Committee. This date was selected for the convenience of those who will attend meetings of the American Physical Society in Montreal, June 19–21, and of the American Society for X-Ray and Electron Diffraction near Montreal, beginning June 23. In addition to contributed papers in the field of solids, the program will include four invited papers: "Diffraction of Neutrons in Crystals," F. Seitz; "Theory of Crystal Rectifiers With Application to Copper Oxide," J. Bardeen; "The Relaxation Spectrum of Metals," C. Zener; and "Nuclear Magnetic Resonance Absorption in Solids and Liquids," E. M. Purcell.

Members of the Organizing Committee of the Division are: T. A. Read, F. Seitz, W. Shockley, S. Siegel, R. Smoluchowski, and C. Zener.

The American Iron and Steel Institute will hold its 55th general meeting in New York at the Hotel Pierre on May 21 and at the Waldorf-Astoria on May 22. One of the features of the program will be the first Charles M. Schwab Memorial Lecture, to be delivered by Eugene G. Grace, Bethlehem Steel Company. Four technical sessions are planned as follows: "Raw Materials," "Coke Ovens, Blast Furnaces

and Steelmaking Furnaces," "Shaping and Forming," and "General Metallurgy." Members are urged to address all communications with reference to luncheon and dinner reservations to: S. A. Maxon, Assistant Secretary, American Iron and Steel Institute, 350 Fifth Avenue, New York 1, New York.

Recent Deaths

Herbert S. Jennings, 79, research associate at the University of California since 1938 and professor emeritus of zoology at Johns Hopkins University, died April 14 in Santa Monica, California, after a year's illness.

Halsey J. Bagg, 57, research biologist who had devoted much of his life to the study of cancer, died April 13 in Yorktown Heights, New York.

William Stanley Marshall, 80, professor emeritus of zoology at the University of Wisconsin, died March 17 in Madison. He published many papers on the anatomy and embryology of insects. A collection of Wisconsin beetles, which he assembled, was left to the University of Wisconsin.

I. Seymour A. Hadwen, 70, former director of the Department of Pathology and Bacteriology, Ontario Research Foundation, and past-president of the American Veterinary Medical Association, died April 18 in Toronto.

Make Plans for—

New York State Geological Association, 19th field meeting, May 9–10, New York City.

Federation of American Societies for Experimental Biology, May 18–22, Chicago, Illinois.

American Association of Cereal Chemists, 32nd annual meeting, May 19–23, Hotel President, Kansas City, Missouri.

American Oil Chemists' Society, 38th annual meeting, May 20–22, New Orleans, Louisiana.

American Society of Mechanical Engineers, oil and gas power 19th national conference, May 21–24, Cleveland, Ohio.

COMMENTS
by Readers

A number of biological papers involving work in which a centrifuge is used are published each year. In an appreciable percentage of these, reference to the amount of centrifuging to which a given material is subjected is presented in terms of duration of centrifuging and the speed of the centrifuge. Such figures, alone, are quite meaningless. Centrifuging data should include duration of centrifuging and the magnitude of the applied centrifugal force. It is possible to centrifuge material at 3,000 r.p.m. (or even at 3,000 r.p.s.) and subject it to little or no centrifugal force, if the material is near or at the center of rotation.

The centrifugal force, in terms of gravity, can be easily calculated if one knows the speed of the centrifuge and the distance of the material from the center of rotation. Heilbrunn (1921) gives the formula

$$c' = \frac{4\pi^2 n^2 r}{g},$$

where n = the number of revolutions per second, r = the distance of the material from the center of rotation in centimeters, g = the gravitational constant, and c' = the centrifugal force in terms of gravity. The figure 39.478 may be substituted for the constant $4\pi r$. Shapiro (1935) has published a useful monogram for obtaining c' if n and r are known.

It is important to stress the fact that r represents the distance of the material from the center of rotation and not the length of the centrifuge arm or the external radius of the centrifuge. The centrifugal force at the outer periphery may be far greater than the effective force, since the material being centrifuged is nearer the center of rotation by the thickness of the outer wall of the centrifuge plus the thickness of the bottom of the centrifuge tube plus the thickness of the layer of supporting medium (if present).

Furthermore, it is not sufficient to state the speed of the centrifuge and the type of centrifuge employed, since most centrifuges have interchangeable heads of different diameters. It is true that, for any given centrifuge with a given head, the speed of rotation and the duration of centrifuging are the variables and the distance of the material from the center of rotation is usually constant. Nevertheless, the latter can be varied by changing the centrifuge head or by altering the method of suspending the material in the centrifuging medium.

Editors could do much to remedy the present situation by insisting that authors either state the centrifugal force employed or give both the speed of the centrifuge and the effective distance from the center of rotation. The former procedure is definitely preferable, however, since it is more concise, saves the reader a task of calculation, and avoids the possibility of subsequent misquotation in terms of centrifugal speed alone.

If the centrifugal force employed in a given set of experiments, particularly on such material as living marine egg cells, is unknown, it is frequently impossible to repeat these experiments and obtain the same result. Rate of sedimentation of the granules and vacuoles of living cells under low centrifugal forces is markedly retarded by redistribution of these inclusions by Brownian movement, as Howard (1931) carefully pointed out.

Among the numerous pieces of work on biological material marred by the oversight of stating centrifugal speed rather than centrifugal force, or entirely omitting mention of magnitude of centrifugal force employed, are those of Boveri (1910), Hertwig (1904), Morgan (1935, 1937), Parseval (1922), Raven (1938), Ries (1939), Wilber (1945), Wilson (1929, 1930), and many others. (DONALD P. COSTELLO, *Department of Zoology, University of North Carolina, Chapel Hill.*)

TECHNICAL PAPERS

Effect of Intraperitoneal Injection of Malignant Urine Extracts in Normal and Hypophysectomized Rats

HOWARD H. BEARD, BERNARD HALPERIN, and SAMUEL A. LIBERT[1]

Department of Biochemistry, The Chicago Medical School

Lipid extracts of normal liver tissue and those from histologically normal liver and other tissues from malignant patients, when injected into rats and mice, cause the appearance of tumors in a number of the animals (*3*). The active factor resides in the nonsaponifiable sterol fraction.

Some time ago we began a study of alcohol-ether extracts of known malignant urines with the hope of producing tumors in rats receiving 2 cc. of these extracts, equivalent to 100 cc. same ratios in the control rats with no injection. This constitutes a biological test of malignancy. In 26 normal urine extracts the test was negative (a decrease of not more than 20 per cent from the controls). The average per cent increase in weight of the organs in these 40 cases over that in the controls was as follows: spleen, 39; male gonads, 55; and female gonads, 72. There was intense hyperemia in the spleen and hyperplasia and intense spermatogenesis in the testes.

In 32 urines from patients whose diagnosis was unknown to us at the time the tests were made, there were 6 positive tests, one each from cancer of the breast, rectum, stomach, prostate, colon, and a malignant melanoma. In the remaining 26 cases all were normal or nonmalignant, and the tests in all were negative. These results confirm those of Carratala, Roffo, and Krebs and Gurchot (*1*) in this connection.

The malignant extracts gradually lose their potency if allowed to stand some time in the ice chest. The average

TABLE 1

Normal rats								Hypophysectomized rats								
Ext. No.	Rat (grams)	Spleen (mg.)	Gonads (mg.)	R/S	R/G	Decrease (%) R/S	Decrease (%) R/G	Rat (grams)	Spleen (mg.)	Gonads (mg.)	R/S	R/G	Decrease (%) R/S	Decrease (%) R/G	Clinical diagnosis Ca of:	Age of extract (mos.)
C	87	267	90	326	966			69	180	282	383	245				
21	85	535	252	158	337	52	65	69	206	292	335	236	13	4	Bronchiogenic Ca	1
C	104	966	1,403	107	74			104	966	1,403	107	74				
21	95	1,073	1,903	89	50	17	32	98	941	1,094	104	90	0	0	Bronchiogenic Ca	4
C	115	868	1,105	132	104			69	180	282	383	245				
28	124	900	2,060	137	60	0	42	80	224	197	357	406	7	0	Breast	1
C	112	1,046	1,501	107	75			112	1,046	1,501	107	75				
28	132	1,216	2,321	108	57	0	24	101	832	1,350	121	74	0	0	Breast	4
C	97	333	87	291	1,114			109	850	1,395	128	78				
34	89	669	335	133	266	54	76	110	785	1,415	140	78	0	0	Prostate	1
C	95	903	1,381	105	69			95	903	1,381	105	69				
34	127	1,365	1,900	93	66	11	0	98	510	1,384	192	71	0	0	Prostate	4
C	107	483	200	221	535			111	863	1,175	128	94				
37	107	748	530	143	201	35	62	123	915	1,410	134	87	0	7	Mediastinum (Mtas to spine)	1
C	81	680	1,190	119	68			81	680	1,190	119	68				
37	109	1,160	1,875	93	58	22	15	83	660	946	126	88	0	0	Mediastinum (Mtas to spine)	4

of original urine. It was found, however, that 2 to 4 days after injection of the extracts there was an enlargement in the spleen and/or gonads. In 39 out of 40 known malignant extracts the decrease in the body weight:spleen and body weight:gonad ratios ranged from 20 to 80 per cent below these

[1] The authors wish to thank F. C. Koch, director of the Armour Laboratories, for the suggestion to use hypophysectomized rats and for instruction in the use of the Ingle technique of hypophysectomy.

decrease in the R/S ratios in fresh extracts was 47 per cent compared to only 17 per cent at the end of four months. These values for the R/G ratios were 61 and 24 per cent.

We believe that a substance, X, which is present in the blood and urine of all malignant patients so far tested, is either a sterol or a sterol-protein complex. Roffo, and Krebs and Gurchot, further stated that a gonadotropic hormone was responsible for the results of the biological test. In order to in-

vestigate this point a study was run in which known malignant urine extracts were injected into normal and hypophysectomized rats. The results obtained are listed in Table 1. In this study, 39 out of 40 known malignant urine extracts gave a positive biological test two days after injection. In 32 urines of unknown diagnosis the test was positive in 6 malignancies and negative in 26 nonmalignancies. All urine extracts from normal individuals and other nonmalignant cases were negative.

The following views are supported by the results:

(1) Malignant urine extracts lose about 60 per cent of their ability to give the test after standing in the ice chest for four months.

(2) The biological test is *negative* in the hypophysectomized rat.

(3) *All malignant urines so far tested by ourselves (with one exception) and others* contain a substance, X, which is protein-sterol or sterol in nature and which stimulates the rat pituitary to produce increased amounts of another substance, Y, possibly a gonadotropic hormone, which is then responsible for the biological test for human malignancy.

The idea given in (*3*) is confirmed by Gurchot, Krebs, and Krebs (*2*), who stated: "The experiments herein described indicate that normal human pregnancy trophoblast (from human placental tissue), when grown in the anterior chamber of the eyes of rabbits, behaves like a malignant tumor grown in a similar medium. Our experiments, as well as those of others, suggest that all malignant tumors, regardless of their protean character, are fundamentally trophoblastic."

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Serum Phosphatases and Alloxan Diabetes[1]

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Alloxan diabetes was produced in adult male albino rats by a single subcutaneous injection of 16 mg. of alloxan monohydrate for each 100 grams of body weight. The animals were housed in metal cages, 6 to a cage, and fed Purina Fox Checkers with tap water *ad lib.* Of 61 animals used, 6 per cent were unaffected by the treatment; 10 per cent recovered from an early hyperglycemia; 20 per cent developed hyperglycemia and died within three days. The remaining 64 per cent survived for long periods and exhibited hyperglycemia, glycosuria, lipemia, and ketonuria. Polyuria and polydipsia were marked, and there was progressive weight loss to the extent of 50 per cent of the original weight in three weeks.

Specimens of tail blood were obtained periodically for the estimation of blood glucose, serum inorganic phosphorus, and acid and alkaline phosphatases. Blood sugar was estimated by the micromethod of Reinecke (*5*). Serum phosphorus and phosphatases were determined by the method of Shinowara, *et al.* (*6*) as modified by Gould and Schwachman (*3*). Acid and alkaline phosphatases were estimated at pH 5.3 and pH 9.3, respectively. The normal mean values, previously determined in fasted animals, were: blood sugar, 117 mg./100 ml.; serum inorganic phosphorus, 9.0 mg./100 ml.; serum acid phosphatase, 3.2 units/100 ml.; and serum alkaline phosphatase, 113 units/100 ml.

Six animals were used for each experiment and the results averaged. Table 1 presents the findings in a representative group.

There is a rapid, progressive rise in blood sugar. This exceeds 400 mg. per cent at the end of two days and is maintained thereafter with only slight fluctuations. The initial transient rise in blood sugar in rabbits noted by some observers (*4*) and attributed to the release of adrenalin was not observed in the present experiment. In our subsequent experiments, not reported here, in which the dosage of alloxan was greater, such an early transient blood sugar rise was observed. The acid phosphatase falls quickly to about 25 per cent of the initial level and returns to normal in three days. Alkaline phosphatase shows a similar initial decline which is restored within 12 hours. This is followed by a progressive increase over the next two weeks, when values in excess of three times the normal level are reached. Serum inorganic phosphorus is not greatly altered, but nearly all values found after the injection of alloxan are greater than the initial levels.

TABLE 1

Effect of Alloxan on Blood Sugar, Serum Phosphatases, and Inorganic Phosphorus

Time after administration of alloxan	Blood sugar (mg./100 ml.)	Serum alkaline phosphatase (units/100 ml.)	Serum acid phosphatase (units/100 ml.)	Inorganic phosphorus (mg./100 ml.
0 hrs.	123	109	3.6	8.3
2 "	166	—	—	—
3 "	216	56	0.93	—
6 "	—	64	1.0	10.9
9 "	250	89	1.3	9.9
12 "	310	105	1.6	9.1
24 "	380	125	1.7	8.4
2 days	464	154	1.5	8.6
3 "	440	179	3.7	8.9
4 "	425	205	4.2	9.8
5 "	426	223	4.2	10.5
7 "	358	177	4.1	9.4
8 "	412	250	4.0	9.9
14 "	444	365	4.6	9.0
21 "	420	371	3.7	9.3
42 "	437	380	4.4	10.1

The hyperglycemia and ketonuria which develop are easily controlled with insulin. A single subcutaneous injection of 0.4 units of crystalline zinc insulin restores the blood sugar to within normal levels in three hours. This is accompanied by a 30 per cent decline in both acid and alkaline phosphatases. At the end of 24 hours all values are restored to the diabetic levels. In order that the effect of insulin could be observed over

[1] This work is part of Project M.P. 80, conducted with the assistance of a grant to M. M. Cantor from the Division of Medical Research, National Research Council, Ottawa.

a longer period, three doses of 0.4 units of insulin were injected at three-hour intervals. The averaged results in four animals are presented in Table 2.

Blood specimens obtained 90 minutes after the third injection of insulin show hypoglycemia, reduction of acid phosphatase to 25 per cent of normal, and reduction of the alkaline enzyme to within normal limits. Serum inorganic phosphorus is reduced.

TABLE 2

EFFECT OF THREE DOSES OF 0.4 UNITS OF INSULIN AT THREE-HOUR INTERVALS ON BLOOD SUGAR, SERUM PHOSPHATASES, AND INORGANIC PHOSPHORUS IN ALLOXAN-DIABETIC RATS

Time after injection of insulin	Blood sugar (mg./100 ml.)	Serum alkaline phosphatase (units/100 ml.)	Serum acid phosphatase (units/100 ml.)	Serum inorganic phosphorus (mg./100 ml.)
0 hrs.	425	384	3.9	11.8
1st dose				
1½ hrs.	150	346	3.1	11.1
3 "	154	284	2.3	11.5
2nd dose				
1½ hrs.	77	236	2.0	11.5
3 "	101	197	2.4	9.2
3rd dose				
1½ hrs.	51	161	1.0	10.2
3 "	122	132	1.0	9.8
9 "	410	206	2.3	7.4

Our findings indicate that the development of alloxan diabetes in rats is accompanied by an increase in serum alkaline phosphatase activity and that the administration of insulin produces a decrease in the activity of both the acid and alkaline enzymes. The initial decline in phosphatase activity following the injection of alloxan simulates that produced by the injection of insulin and is attributed to the release of insulin stores in the pancreas. When this supply is exhausted, alkaline phosphatase activity increases and remains elevated, the increase being parallel to the elevation in blood sugar. Both are reduced, again in parallel fashion, by the administration of insulin.

We have been unable to demonstrate any great increase in serum inorganic phosphorus following the administration of alloxan, although nearly all the values found were in excess of the preinjection level, and a few were greatly increased. Following the administration of insulin in the alloxan diabetic animal, reduction in the level of inorganic phosphorus was demonstrated. These findings are in accord with the well-known effect of insulin both in the diabetic and normal organisms (*1, 2*) and suggest that these alterations reflect changes in phosphatase activity.

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The pH Stability of Viruses of Newcastle Disease and Fowl Plague[1]

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The recognition (*2*) of the immunologic identity of the causative agent of avian pneumoencephalitis with that of Newcastle disease revealed the existence of a serious threat to the poultry industry of the United States. The clinical features of the American form of the disease have allayed suspicion of its identity with the classical, hitherto highly virulent Newcastle disease (*1*). The differences between the American and the classical forms may result from the noted marked pneumo- and neurotropism of the virus isolated in this country and the pronounced enterotropism of a European strain of the virus (*7*). In Europe and elsewhere, Newcastle disease has been mistaken for possible forms of fowl plague and vice versa, and immunologic evidence has been obtained to support both dissimilarity (*5*) and similarity (*8*) of these diseases. However, recent immunologic and other comparative studies have provided strong support for the unity of each disease (*4*). The importance of these two diseases, the one a real, and the other a potential, threat to the poultry industry of this country, prompted studies to obtain further information on the relationship of the American and European Newcastle disease viruses and of these, in turn, to the virus of fowl plague.

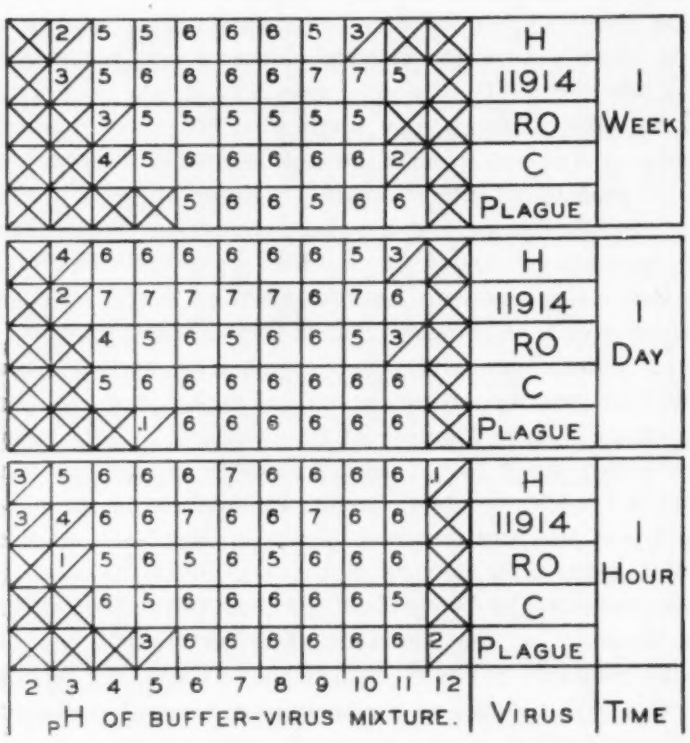
An evaluation by Doyle (*5*) of the effect of marked acidity and alkalinity on the Newcastle virus infectivity indicated greater resistance to the H- than to the OH-ions. The results of Pyl (*10*) in the case of the fowl plague virus showed that maximal stability of the infectivity occurred between pH 6.3 and 9.1 and that the virus was destroyed immediately at pH 4 and 12.7. This pattern was similar for brain and blood virus of chickens infected with the Brescia and Bologna strains of plague virus. These results and those for other viruses (*6, 10*) suggested or showed rather distinctive pH stability patterns.

Evaluations of the pH stability were made on four strains of the Newcastle disease virus, including the Hertfordshire strain (H) of English origin and three strains (11914, RO, and C) isolated from cases of "pneumoencephalitis" in California and provided by J. R. Beach, and on the Dutch East Indies strain of the fowl plague virus. A variant virus (Strain 4395), isolated from the plague virus in the course of other procedures (*9*), was subjected to similar study. The source of the virus used in all tests was the allanto-amnionic fluid of embryonated chicken eggs which had been infected with the respective viruses after 10–12 days of incubation. These materials were admixed in the ratio of 1:99, or, in a few tests, 1:9, with portions of a buffer solution (*3*) having pH values of from 2 to

[1] This work was done as a part of a research project conducted under the direction of a War Department Commission consisting of: Brig. Gen. R. A. Kelser, U. S. Army; B. E. Dyer, U. S. Public Health Service; H. W. Schoening, Pathological Division, Bureau of Animal Industry, U. S. Department of Agriculture; and E. B. Fred, University of Wisconsin.

12; the buffer solutions differed by a gradient of 1 pH and were prepared by the addition of NaOH, HCl, or distilled water so that the final concentrations of buffer salts were the same in all. These mixtures or the dilutions thereof in 1 per cent peptone broth (pH 7.8) were held at 2°–6° C. until used to test for the presence of virus. Infective virus was detected by its activity in 10- to 12-day embryonating chicken eggs following intra-allantoic inoculation. Tests for the virus were conducted at intervals of one hour, one day, and one week following the preparation of the buffer-virus mixtures. The pH values of the mixtures were determined by a glass electrode potentiometer after intervals of one day and one week.

The typical reproducible results obtained with the four strains of the Newcastle disease virus and the fowl plague virus are shown in Fig. 1. These results pertain to virus-buffer



VIRUS NONINFECTIVE.

INFECTIVITY TITER OF VIRUS REDUCED TO THE GIVEN DILUTION INDICATED BY RECIPROCAL OF LOG.

INFECTIVITY TITER OF VIRUS NOT SIGNIFICANTLY REDUCED; INFECTIVITY TITER INDICATED BY RECIPROCAL OF LOG OF THE DILUTION LETHAL FOR EMBRYOS.

FIG. 1

mixtures that were made in the ratio of 1:99. It will be noted that definite variations occurred in stability among the strains of Newcastle virus. In the acid range, two of the California strains (RO and C) showed comparable stability patterns, while one strain of this source was somewhat more resistant to acidity and was comparable to the strain (H) of English origin. All four strains were essentially similar in the presence of alkali after exposure for one hour, while infective virus of two of the strains (English and RO) diminished in concentration after one day, and still further variations were demonstrated after one week. A summary consideration of all four strains shows that after one hour a maximal stability existed over the range of approximately pH 4 to pH 11, while survival was possible over the range of pH 2 to pH 12; that after one week a maximal stability could be expected within at least the scale from approximately pH 5 to pH 9; and that survival of the virus should be anticipated approximately from pH 2 to pH 11. These stability ranges were considerably broader than that demonstrable for the virus of fowl plague.

The plague virus was much more sensitive to an acidic environment than the Newcastle virus, but was not distinctly unlike it with respect to alkali. The plague virus survived in maximal titer, after one week, from pH 6 to pH 11; the same maximal stability was demonstrated after exposure to the various pH conditions for one hour, but at this time infective virus was still present at pH 5 and at pH 12.

The pH values of the virus-buffer mixtures made in the ratio of 1:99 were found to drift toward the pH of the virus material (pH 7.8–8), but after one week this did not exceed 0.25 of one pH value in the extreme of the acid range or 0.5 of one pH value in the extreme of the alkaline range.

The results of a comparative study of the pH stability of the plague virus with that of a variant virus isolated from it are shown in Fig. 2. The ratio of quantity of virus material

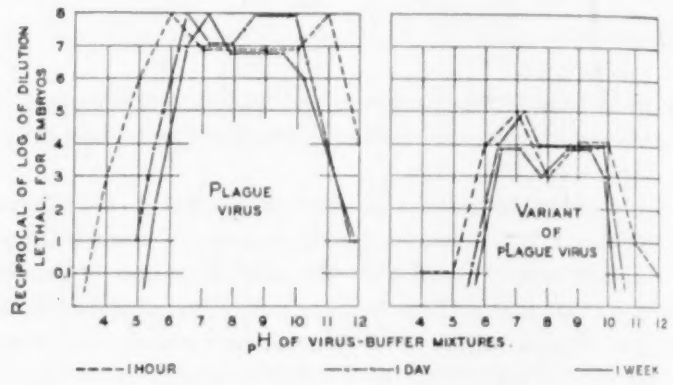

RECIPROCAL OF LOG OF DILUTION LETHAL FOR EMBRYOS
PLAGUE VIRUS
VARIANT OF PLAGUE VIRUS
4 5 6 7 8 9 10 11 12
pH OF VIRUS-BUFFER MIXTURES.
1 HOUR
1 DAY
1 WEEK

FIG. 2

to that of buffer employed here was 1:9. The stability patterns of the infectivity of both of these viruses were essentially similar; the differences that occurred between them are attributed to the lower concentration of the variant strain of virus that was attainable and/or to the ability to demonstrate it in small amounts by the route that was employed to inoculate the embryonated eggs. The differences between this test with the stock or typical strain of plague virus and the results reported heretofore appear accountable to the drift in pH and possibly the other factors associated with the use in the test of 10 per cent virus-infected allanto-amnionic fluid in the virus-buffer mixtures.

These observations are believed to reveal a close relationship among four strains of Newcastle disease virus, a distinct diversity between the virus of Newcastle disease and that of fowl plague, and a similarity between the fowl plague virus and a variant virus derived from it. The pH-stability patterns of a representative strain of the virus of classical Newcastle disease and of strains of virus from cases of so-called pneumoencephalitis in California are believed to confirm the immunological evidences of the identity of the causal agents of these two diseases which possess divergent tropisms. Likewise, the patterns obtained for a classical strain of the virus of fowl

plague confirmed information on its immunological identity with a variant virus of low virulence isolated from it. The results obtained with the fowl plague virus are in agreement with those recorded by Pyl. The stability patterns appear to be useful in the identification of the virus of Newcastle disease and of fowl plague.

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Effect of Gamma Globulin on Circulating Human Complement

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Haynes and Evans Memorials, Massachusetts Memorial Hospitals, and *Department of Medicine, Boston University School of Medicine*

It has been shown by Davis, Kabat, Harris, and Moore (*1*) that the gamma globulin fraction of human serum separated by electrophoresis displays the same tendency to interfere with the activity of alexin as do globulin solutions prepared by other methods. These investigators noted that this effect was diminished or reversed by the addition of albumin and certain other serum proteins. However, since human gamma globulin is being used clinically for the prevention and modification of rubeola and infective hepatitis and has been under study as a therapeutic agent in scarlet fever, it appeared important to ascertain whether patients treated with this material exhibited any changes in the complement levels of their sera. This clinic has participated in a study of the therapy of scarlet fever with human gamma globulin, and the opportunity to study this question thus presented itself.

Methods

Normal gamma globulin was furnished by Sharp and Dohme. This fraction was prepared under the direction of E. J. Cohn and his associates in the Department of Physical Chemistry, Harvard Medical School, from pooled human plasma collected by the American Red Cross. Only lots containing 45 or more units of streptococcal antierythrogenic antibody/ml. were employed. In the course of other investigations with this material it was found to be anticomplementary in the test tube even after the addition of considerable amounts of human albumin (*2*). As stated previously, in the hands of Davis and his colleagues, human albumin decreased or abolished the inactivating effect of globulin on alexin. It is probable, therefore, that the preparation administered in this study was anticomplementary in high titer. Nine patients, whose weight exceeded 60 pounds, received intramuscular injections of 60 ml. of the globulin, while one child weighing 50 pounds was given 50 ml.

Blood was obtained prior to the administration of globulin and at 2-, 4-, 8-, 12-, 16-, 20-, 24-, 36-, and 48-hour intervals thereafter. In each case, one specimen was omitted, withdrawal of blood being avoided in the hours after midnight. However, the schedule was so arranged that no interval was consistently neglected. The sera were separated immediately after bleeding and promptly frozen. Complement titration was carried out with sheep erythrocytes and rabbit amboceptor, 2 units of amboceptor being added to 0.5 ml. of 5 per cent sheep erythrocytes. Determinations were made in saline containing .01, .02, .03, .04, .05, .06, .07, .08, .09, .10, .20, .30, .40, and .50 ml. of the serum being tested, respectively. All tubes contained a total volume of 2.5 ml. and were incubated for one hour at 37°C. before reading. On the basis of rather extensive experience with this method it has been found that the alexin titer (50 per cent hemolysis) of human serum is usually 0.03–0.04 ml. It has been shown repeatedly with this technique that in certain diseases the complement titer may be depressed to 0.10 ml. or more (*5*).

Results

The sera of the 10 patients examined before, and at frequent intervals for 48 hours after, the injection of normal gamma globulin all contained normal levels of complement; 0.04 ml. or less produced 50 per cent hemolysis regularly. Thus, no difference could be detected between control and postglobulin injection alexin titers.

Discussion

Because of its high antibody content (*2*), human gamma globulin is being used as a prophylactic and therapeutic agent in certain diseases (*4*). In light of the known complement-binding character of this material, the sera of patients injected with globulin were examined for alexin levels. No change was demonstrated. In view of the albumin content of human serum, the dilution by the circulating blood, and possibly the relatively slow rate of absorption following intramuscular injection, it is not surprising that gamma globulin, in the dosages usually employed, produced no demonstrable alteration in complement activity when administered intramuscularly to man. If preparations suitable for intravenous injection become available, the possibility that they may produce complement depression when administered by this route should merit investigation.

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[1] The authors are grateful for the cooperation of Drs. E. J. Cohn and J. L. Oncley, Department of Physical Chemistry, Harvard Medical School.

IN THE LABORATORY

False Disinfection Velocity Curves Produced By Quaternary Ammonium Compounds

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Quaternary ammonium compounds are being offered as disinfectants for the medical professions, as bactericides for the sanitization of eating utensils and drinking glasses, and as germicides for general use. The more widely used commercial bactericides of this class are Hyamine 1622 (p-diisobutyl-phenoxy-ethoxy-ethyl-dimethyl-benzyl ammonium chloride monohydrate) and the apparently identical or very similar Phemerol (p-tert-octyl-phenoxy-ethoxy-ethyl-dimethyl-benzyl ammonium chloride monohydrate); Roccal and the identical or closely related Zephiran; Emulsept; Q.A.C.; and Teramine.

Before recommending to the State Department of Health that these compounds be approved as bactericides, additional studies of their efficiencies and limitations were made. When tested by the official Food and Drug Administration method for evaluating antiseptics and disinfectants (*3*), all appear to justify the very high "phenol coefficient" values of 250 to 625 against *Staph. aureus* (*1*) and approximately one-half as great against *E. typhosa* (*2*). The end points obtained when the F.D.A. method was used were very irregular, and plate counts of bacterial populations exposed to quaternary ammonium compounds revealed a very high initial velocity of disinfection:

$$K = \frac{I}{\text{time}} \cdot \log \frac{\text{initial number of organisms exposed}}{\text{survivors}}.$$

This was followed by a rapidly decreasing value of K. When the logarithms of the survivors, as determined by plate counts, were graphed against time, very steep curves were obtained for the first few minutes. The data presented in Fig. 1 are typical. In some instances, particularly when the bactericidal activity was tested in the presence of some additional organic material such as milk, the plate-count numbers again increased after several days and proteolytic decomposition of the milk took place.

Experimentally, it has been found that the presence of sterile evaporated milk allows the growth of organisms exposed to solutions of quaternary ammonium compounds, while parallel inoculations into broth fail to grow.

The shape of the death-rate curve may be somewhat influenced by the rapid removal of the quaternary ammonium compound from the solution. When used in the dilutions their phenol coefficient numbers would indicate them to be efficient bactericides, these compounds are rapidly removed from solution by particulate or organic materials. Also, the hypothesis is advanced that the very high phenol coefficient numbers previously reported for the quaternary ammonium compounds reflect the sum of the agglomeration of the organisms, and their bacteriostatic action in addition to their bactericidal action. These compounds are extremely surface-active cationic detergents, and the clumping of treated organisms, with their adhesion to glass surfaces, has been observed experimentally.

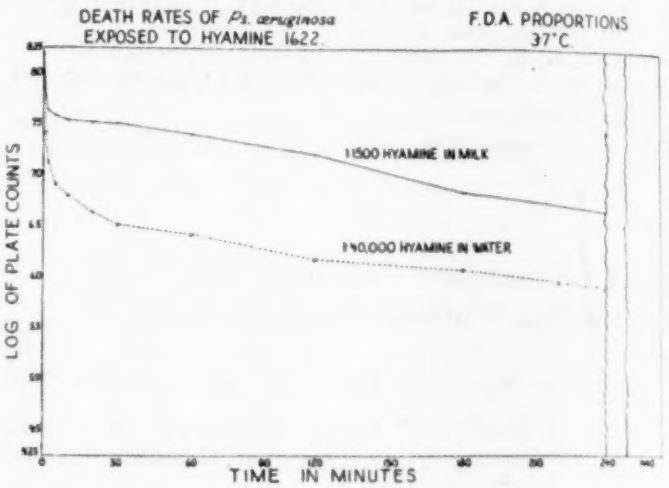

FIG. 1

In tests by the F.D.A. technic, the 1/100-ml. loop might not pick up a clump of agglomerated organisms which tend to adhere to the surface of the tube; if picked up, such a clump might remain adherent to the loop when it was immersed in the broth subculture; and if the coated and agglomerated organisms were placed in broth, in which no additional particulate material was present, they might remain in a state of bacteriostasis and fail to give rise to growth. In the case of plate counts in agar, many viable organisms in one clump would give rise to only one colony and hence would be read as only one viable inoculum.

Since it appears that the tendency of organisms to agglomerate and adhere to surfaces, following exposure to dilute solutions of the quaternary ammonium compounds, has influenced the end points obtained with the F.D.A. method and the apparent velocity of disinfection when plate counts were made, both the bactericidal efficiencies and the very favorable toxicity indices of these compounds must be re-evaluated.

In some clinical applications it is possible that a surface-active bacteriostat, of very low toxicity to tissues, may be more desirable than an active bactericide which decreases tissue vitality. Also, it has yet to be demonstrated whether viable organisms coated with quaternary ammonium compounds are infective or are readily destroyed by the natural defense mechanisms of the body.

The data thus far obtained indicate that, when employed in sufficient concentrations and in the absence of large amounts

of particulate or organic materials, the quaternary ammonium compounds probably do disinfect.

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The Maillard Reaction in Microbiological Assay[1]

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In 1912 Maillard (*1*) pointed out that solutions containing amino acids and reducing sugars turn brown when heated. Although this browning reaction has recently been recognized to be of the greatest importance in nearly all industries concerned with materials of biological origin, including foods, it is still little understood because of its complexity. It occurred to the writers that further insight into the Maillard reaction might be gained through use of the microbiological assay technique, since the latter involves the autoclaving of solutions containing amino acids and dextrose (a reducing sugar) under conditions favorable to the Maillard reaction.

Accordingly, the customary casein hydrolysate medium was prepared for tryptophane assay with *Streptococcus faecalis* in such a way that the reducing sugar component of the medium (dextrose) could be autoclaved separately from the rest of the medium for comparison with a "normal" series, using medium containing identical ingredients but autoclaved in the presence of dextrose in the customary manner.

The growth curves obtained are shown in Fig. 1. Good growth was obtained by the standard procedure (Curve A), but still better growth was obtained in the medium prepared by autoclaving the dextrose separately from the rest of the medium and combining aseptically after cooling (Curve B). These results have been repeated and are reproducible.

It thus appears likely that optimal growth may seldom be reached in microbiological assays, due to the effects of the Maillard reaction. This would not be discovered in recovery tests, since both standard and unknown series would be autoclaved alike. The question arises, however, whether this apparent accuracy of the microbiological assay can always be relied upon, in view of the possibility that standard and unknown samples might differ in their ability to alter the influence of the Maillard reaction upon growth.

Since sucrose is not a reducing sugar and does not readily take part in the Maillard reaction, it was thought that sucrose might be preferable to dextrose, if satisfactory growth were obtained in a medium containing sucrose. Accordingly, a third series was prepared and run simultaneously with the assays shown in Fig. 1. In this C. P. sucrose replaced the dextrose ordinarily used but at one-half equimolar concentration (final concentration of sucrose in the medium, 1/12 M). Here again the growth obtained was better than "normal"; in fact, the growth curve obtained with sucrose in the medium was identical with Curve B (Fig. 1).

A certain amount of browning during autoclaving is commonly accepted as being inevitable in microbiological assay; however, our media using either sucrose autoclaved with the medium or dextrose autoclaved separately were *water white*. Compared with these, the normal medium transmitted 84.5 per cent as much light at 610 mμ, the decrease in transmission being due to the browning which occurred during autoclaving.

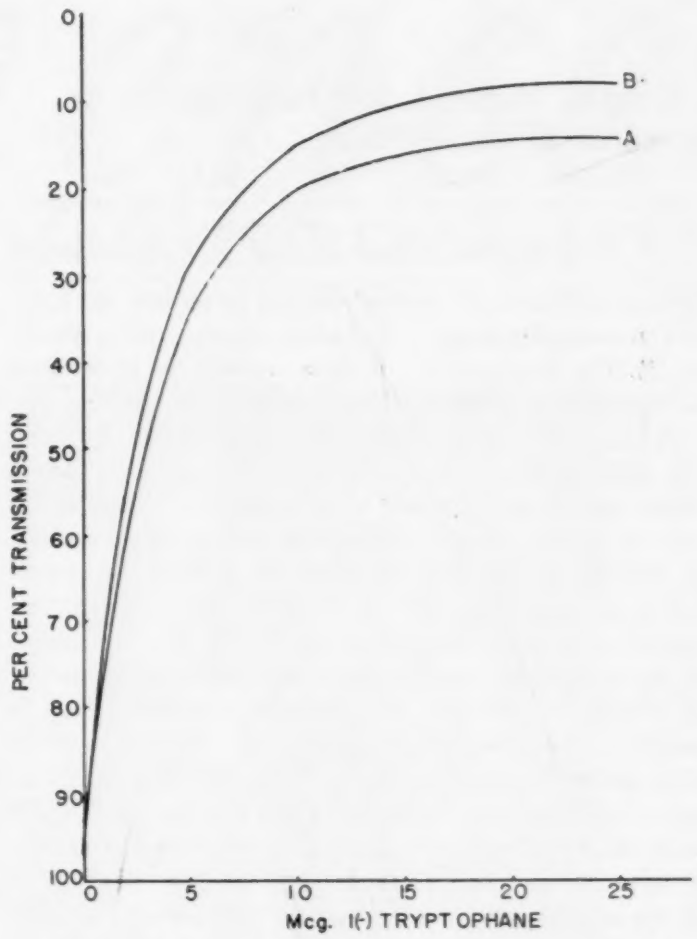

Fig. 1. Growth curves for tryptophane assay using *Str. faecalis*.

Whether the poorer growth obtained by the customary procedure is due to destruction of nutrients or production of growth inhibitors has not yet been determined. The Maillard reaction produces an increase in acidity, and the possibility that this may be responsible for the reduced growth has not been overlooked. The fact that the greatest differential in growth occurs at the higher growth levels lends support to this possibility. The actual difference in acidity due to browning was rather slight, however, amounting to a difference of only 0.96 ml. of 0.1 N acid in the uninoculated blank tubes, which was responsible for a difference in pH of only 0.2 (Curve A medium, pH 6.96; Curve B medium, pH 7.16).

The possibility that these results might be a peculiarity of the tryptophane assay, due to destruction of tryptophane during autoclaving, was ruled out by another series of assays. In these, graded levels of l-tryptophane solution were autoclaved *separately* before adding to the autoclaved media.

[1] Published with the approval of the director of the Colorado Agricultural Experiment Station, as Scientific Journal Series No. 235.

Again, the same results were observed: the greater the extent of browning which occurred during autoclaving, the less the subsequent growth obtained with a given level of tryptophane.

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A Simple Method for Rearing Blowflies Without Meat[1]

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The methods used for rearing blowflies to be used in experiments on insect physiology or toxicology are reviewed by Woodbury (*2*). The disadvantages of these methods, in all of which meat or fish are used for larval food, are twofold: (1) Meat and fish are not always readily or cheaply obtainable, and (2) rotting of the flesh during larval feeding results in unpleasant odors.

Many expedients have been tried to minimize the escape of odors, but none of these is entirely satisfactory. Recently Hill, Bell, and Chadwick (*1*) have solved the problem by rearing blowflies on a sterile synthetic medium. While this method does eliminate most of the odors and allows control of the larval food, it involves the compounding and autoclaving of the medium. These procedures are time consuming and may even be impossible without technical assistance. Accordingly, a simple method for rearing blowflies in quantities, without using putrid meat, seemed desirable. *Phormia regina* Meigen was used in most of the tests, but other species of blowflies could undoubtedly be reared as well.

In the method developed the medium used for rearing larvae is ordinary commercial kibbled dog biscuit.[2] The bone-shaped biscuit can also be used but must be broken into small pieces.

Rearing containers are one- and two-quart Mason jars or gallon mayonnaise jars. In a jar, dog biscuit to a depth of about two or three inches is covered with water and allowed to stand for about two minutes. The water is then poured off, and eggs or young larvae of the blowflies are added. The jar is capped with a circle of fine-mesh wire cloth held in place by a ring cap. This allows air to enter freely and excess moisture to escape, while preventing the escape of the larvae. The larvae generally do considerable migrating, both in the mass of dog biscuit and on the walls of the jar.

When the larvae are nearly full grown, the jar is almost filled with coarse sawdust. In this, the larvae crawl about and pupate. The sawdust and pupae are then removed and the pupae sorted out for emergence, or the sawdust is left in the jar and the flies allowed to emerge there. Flies are removed from the jar by attraction to a light source.

Correct moisture content of the larval medium is an important consideration. This depends on the particle size: the smaller the particles, the less water needed for optimum moistness. Since different brands of dog biscuit and even different samples of the same brand vary considerably in particle size, the technique of moistening the material must be acquired by experience. If the medium is too moist, the larvae leave the food quite early and crawl about in the film of water on the inside of the bottle. In this case it is necessary to add a layer of sawdust, about one inch deep, over the dog biscuit. This usually takes up the moisture and drives the larvae back to the food.

If the dog biscuit is relatively coarse, the larvae will crawl about in it freely to a depth of three to four inches. If, on the other hand, the dog biscuit is fine, the larvae are restricted to the topmost layer and go only about one inch deep. Since their feeding ultimately causes the medium to pack, whatever its original consistency, the dog biscuit is utilized only to a depth of about two inches. Thus, increased production of flies cannot be obtained by increasing the depth, but only by using more jars or jars of larger diameter.

The production of large, well-formed flies is obviously dependent upon the density of larval population. Thirty to 40 grams of dog biscuit will produce 100 such flies. In a two-quart Mason jar we use about 250 grams of dry dog biscuit, and this produces up to 1,000 flies. Under these conditions, 100 flies are produced at a cost of about $.01, using dog biscuit purchased at a retail price of $.60–$.70 for 5 pounds. If purchased in bulk at wholesale rates, the cost would obviously be much lower.

Adult blowflies are kept in screen cages, where they are supplied with water, sugar, and moistened dog biscuit. The latter is both the oviposition medium and protein food necessary for oviposition. Since blowflies usually will not oviposit on freshly moistened dog biscuit, this material is allowed to remain moist a day or two prior to its use in the cages. If the atmosphere is dry, the dog biscuit is kept damp in the cages by placing it in a finger bowl lined with paper toweling on which a bottle of water is inverted.

Whether blowflies reared on meat will oviposit on moistened dog biscuit has not been determined. In earlier work, the eggs were collected on meat and transferred to dog biscuit for rearing only; thus, when the latter was tested for oviposition, it was tried with flies reared on it. Also tested for oviposition were nutrient agar and filter paper soaked in a strong nutrient broth kept moist by inverting a bottle of water on it. Blowflies fed on both of these but oviposited only on the filter paper. The number of eggs laid on the filter paper, however, was not great enough to warrant continuation of the tests.

This method for rearing blowflies makes possible the production of numbers of large flies with little apparatus and expense. Strangely, the moistened dog biscuit does not develop any objectionable odors while the larvae are feeding, the total lack of ammonia being particularly surprising. Odors that develop during the pupal period are held in the bottles by the sawdust. Thus, the rearing containers may be kept in an office or laboratory, no provisions being needed for air conditioning. Since no autoclaving or special preparation of media are needed, the method is very simple, and the relative constancy of composition of dog biscuit assures that the flies are physiologically quite uniform.

[1] The technical assistance of Mr. Arnold Hultquist in testing this method is gratefully acknowledged.

[2] Brands used successfully in this laboratory are Milk Bone (National Biscuit Company), Daily (The Great Atlantic and Pacific Tea Company), and Kibbies (Morton's Dog Food Company, Minneapolis).

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